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EFFECT OF ACUTE APPENDICITIS AND OF LOBAR PNEUMONIA ON THE THORACIC AND ABDOMINAL RESPIRATORY MOVEMENTS IN CHILDREN

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CHICAGO

It is common knowledge that the movement of the abdominal wall during respiration may be restricted in acute appendicitis. This study was undertaken to determine by an objective method the relative frequency of this restriction, and its value and limitations as an adjunct in the diagnosis of acute appendicitis in children.

PROCEDURE

For some years, patients presenting abdominal signs or symptoms suggesting the presence of appendicitis were studied. Other patients also were observed as controls.

The respiratory movements of the abdomen and of the chest with the child in the supine position were recorded simultaneously on a smoked drum, and the heights of the two curves were compared.

The pneumograph which I employed was made from a light coil spring 1 inch (2.5 cm.) in diameter and about 6 inches (15 cm.) long, wrapped closely and sealed in thin rubber sheeting. The resulting tube was then closed at one end with a cork and hermetically connected from the other end by rubber tubing to a recording tambour of the Marey type. (This pneumograph was somewhat similar to the one described by G. W. Fitz in 1896,[1] but he used a piston recorder.) A length of heavy twilled cotton tape was attached to each end of the tubular pneumograph. A sharp-pronged buckle was attached to one of these lengths of tap for fastening it about the chest or abdomen.

In this study one pneumograph was fastened under very moderate tension about the chest at the level of the nipples, and another was similarly fastened about the abdomen at the level of the umbilicus. The recording apparatus was so designed that equal increases in the circumference of the chest and abdomen from the resting position caused approximately equal excursions of the writing levers. The arrangement of the apparatus was such that the ascending limbs of the

From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital.

1. Fitz, G. W.: A Study of Types of Respiratory Movements, J. Exper. Med. 1:677, 1896.

curves recorded on the drum represented inspiration, and the descending limbs, expiration.

Figure 1 shows the apparatus as used.

The clinical data presented in this paper were for the most part taken from the notes made by various physicians of the hospital staff and entered in the routine hospital records.

EXAMPLES OF CURVES

I present here examples of curves obtained in various conditions. The short perpendicular lines drawn across the two curves in each set indicate synchronous points.

Figure 2 shows tracings from the patients in cases 3 and 10 in table 1 (controls) and is representative of the normal. In these two cases it is seen that, as is usually true for normal children, the excursion of the abdominal movement was greater than that of the thoracic movement. In figure 2 *B* is also shown a curve of a single deep inspiration.

TABLE 1.—*Normal Controls*

Case	Age Yr.	Age Mo.	Condition
1	2	3	Recovered from ileocolitis
2	3	9	Recovered from otitis media; general condition excellent
3	4	4	Recovered from bronchitis; no râles; temperature normal, 4 days
4	5	2	Recovered from acute nasopharyngitis; excellent condition; temperature normal, 10 days
5	5	5	Old scar of burn; general condition normal
6	6	7	Phimosis, preoperative; general condition normal
7	7	3	Tonsillectomy 3 months before; general condition normal
8	8	10	Tonsillectomy 8 months before; general condition normal
9	10		Recovered from ileocolitis; general diet for 2 days
10	10	10	Circumcision 2 days before; general condition normal

Figure 3 *A* (case 41, table 2) illustrates the restriction of the abdominal respiratory movement usually found in acute appendicitis.

Figures 3 *B* (case 47, table 2), 3 *C*, 3 *D* (both tracings from the patient in case 27, table 2) and 3 *E* (case 40, table 2) also illustrate this restriction in appendicitis.

In all cases in table 2 (acute appendicitis in fig. 7) the tracings were made preceding the operation and except as follows on the day of operation: In cases 7, 29 and 39 the operation was performed on the next day after making the tracing, and in case 31, on the third day after making the tracing.

Comparison of figures 3 *C* and 3 *D* shows that there was a greater restriction of the abdominal excursion with a larger thoracic excursion when the patient was asleep than when he was awake.

Figure 4 shows tracings from patients with lobar pneumonia. Figure 4 *A* is representative of the typical curve of lobar pneumonia with a pause in the respiratory movement after inspiration and a shorter than

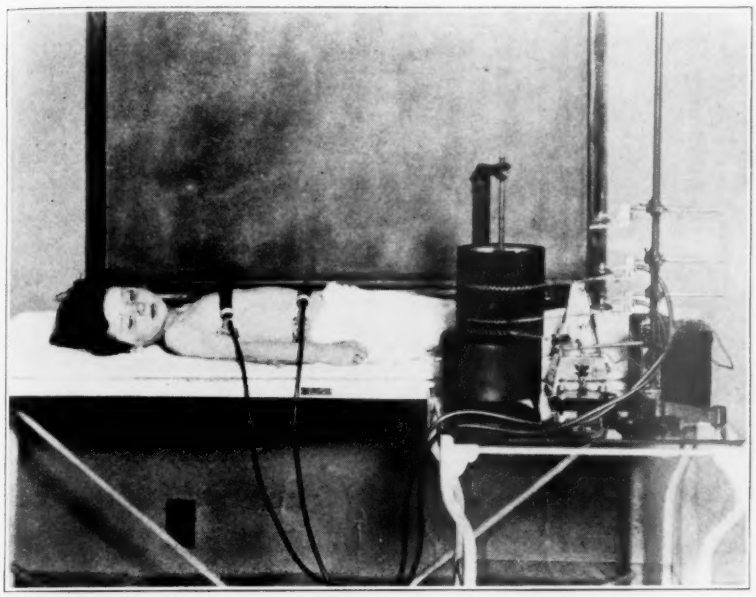

Fig. 1.—Apparatus as used for recording the respiratory movements of the abdomen and of the chest.

Fig. 2.—Tracings from patients: *A*, case 3, table 1; *B*, case 10, table 1.

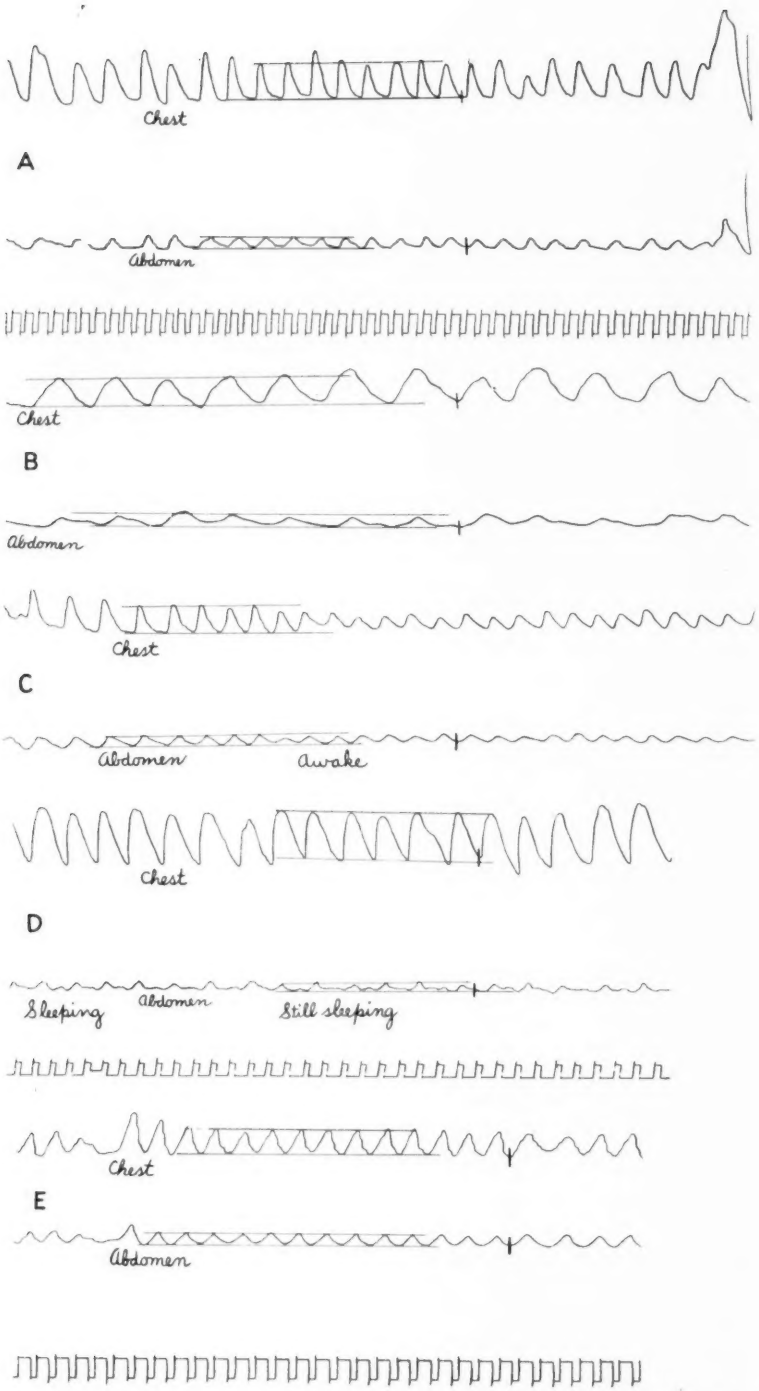

Fig. 3.—Tracings from patients: *A*, case 41, table 2; *B*, case 47, table 2; *C*, case 27, table 2 (made while patient was awake); *D*, case 27, table 2 (made while patient was asleep); *E*, case 40, table 2.

TABLE 2.—*Acute Appendicitis* *

Case	Age Yr.	Age Mo.	Diagnosis in Addition to Acute Appendicitis	Abdominal Respiratory Excursion Less than Thoracic
1	9		Perforated appendix and local peritonitis	Yes
2	7	11	Local peritonitis	Yes
3	4	5	Local peritonitis	Yes
4	9	5		Yes
5	12	8	Perforated appendix and general peritonitis	Yes
6	11	7		Yes
7†	2	9	Perforated appendix and general peritonitis	Yes
8	12		Perforated appendix and abscess	Yes
9	2	10	Perforated appendix and general peritonitis	Yes
10	6			Yes
11	11		Abscess	Yes
12	8		Abscess	Yes
13	8	1	Local peritonitis	Yes
14	8	2	Local peritonitis	Yes
15	4		Perforated appendix and general peritonitis	Yes
16	5	2	Local peritonitis	Yes
17	9	1	Abscess	Yes
18	10		Local peritonitis	Yes
19	3	1	Local peritonitis	No
20	11			Yes
21	7	7	General peritonitis	Yes
22	5		Abscess	Yes
23	7	10	Abscess	Yes
24	4	9	Perforated appendix and local peritonitis	Yes
25	3	8	Perforated appendix and local peritonitis	Yes
26	8	4	Perforated appendix and local peritonitis	No
27	2		Perforated appendix and abscess	Yes
28	9	1	Perforated appendix and abscess	Yes
29†	5		Abscess	Yes
30	11	10		Yes
31‡	11	7	Abscess	Yes
32	9	9		Yes
33	11			Yes
34	10		Local peritonitis	Yes
35	7			Yes
36	2	11	Local peritonitis	Yes
37	5		Abscess	Yes
38	2	9	Perforated appendix and abscess	No
39†	12			Yes
40	6	6	Perforated appendix and abscess	Yes
41	7	9		Yes
42	10		Abscess	No (equal)
43	5			Yes
44	5	9	Local peritonitis	No (equal)
45	10	9		Yes
46	9	9	Local peritonitis	Yes
47	9	6	Local peritonitis	Yes
48	4	9	Perforated appendix and local peritonitis	Yes
49	10			Yes
50	7		Local peritonitis	Yes
51	10	9		Yes
52	6			Yes
53	6	4		Yes
54	11	2		No
55	8	3		Yes
56	8	4		Yes
57	7	4		Yes
58	5		Local peritonitis	No
59	12	1		Yes
60	11			Yes
61	8		Perforated appendix and abscess	No (equal)
62	11	9	Local peritonitis	No
63	9			Yes
64	10	6		No
65	5	3	Perforated appendix and general peritonitis	Yes
66	12		Perforated appendix and local peritonitis	No
67	9			No (equal)
68	8	8	Perforated appendix and local peritonitis	No
69	11			No

* The tracings were all made before the operation and except as noted on the day of operation.

† The operation was done on the day after the tracing was made.

‡ The operation was done on the third day after the tracing was made.

normal pause after expiration. The pause at the end of inspiration caused a flattening of the top of the curve, especially well shown in the abdominal curve in this case. The abdominal and thoracic movements were of approximately equal amplitude. In figure 4 *B* (tracing from a patient with lobar pneumonia on the right side) it may be seen that when the patient was asleep the respiratory curve was regular and without the flattened top from a pause after inspiration and that when the child awoke such a pause immediately appeared. In figure 4 *C* the tracing shows the inspiratory pause to have been absent during quiet

TABLE 3.—*Pneumonia with Abdominal Symptoms*

Case	Age Yr.	Age Mo.	Diagnosis	Abdominal Symptoms
1	10	10	Right lower lobar pneumonia.....	Pain and tenderness
2	13		Left lower lobar pneumonia.....	Tenderness
3	8	9	Upper and lower right lobar pneumonia	Pain, tenderness and rigidity
4	10	6	Postoperative pneumonia.....	Tenderness, left lumbar region
5	11		Right lower (and upper?) lobar pneumonia	Pain with bilateral rigidity
6	4	6	Left lower lobar pneumonia.....	Tenderness; suggestion of rigidity

TABLE 4.—*Conditions with Abdominal Symptoms Not Due to Appendicitis*

Case	Age Yr.	Age Mo.	Diagnosis	Abdominal Symptoms
1	12		Cystinuria, right nephrolithiasis....	Moderate rigidity; tenderness
2	7	9	Acute pneumococcic peritonitis; fibrinopurulent pleurisy; tuberculous mediastinal lymph nodes	Generalized abdominal tenderness, more of lower half, with generalized doughy rigidity
3	3	7	Fracture of left ilium with hematoma	Pain and tenderness, left flank and left inguinal region
4	6	6	Traumatic rupture of kidney; blood clots in urine	Pain, tenderness and rigidity
5	6	9	Traumatic rupture of left adrenal gland with peritoneal hematoma	Pain, tenderness and rigidity

breathing. In figure 4 *D* the appearance of a definite pause in inspiration on awakening from sleep is again shown. These curves seem to indicate that a conscious state is necessary for the production of the inspiratory pause often found in lobar pneumonia.

Figure 5 *A, B, C* and *D* (cases 1, 2, 3 and 6, respectively, table 3) illustrates the observations in cases of pneumonia with abdominal tenderness or signs suggesting acute appendicitis. It is seen that, contrary to the usual finding in acute appendicitis, there is no restriction of the abdominal excursion as compared with the thoracic excursion. This sign if constant should help differentiate this type of condition from acute appendicitis.

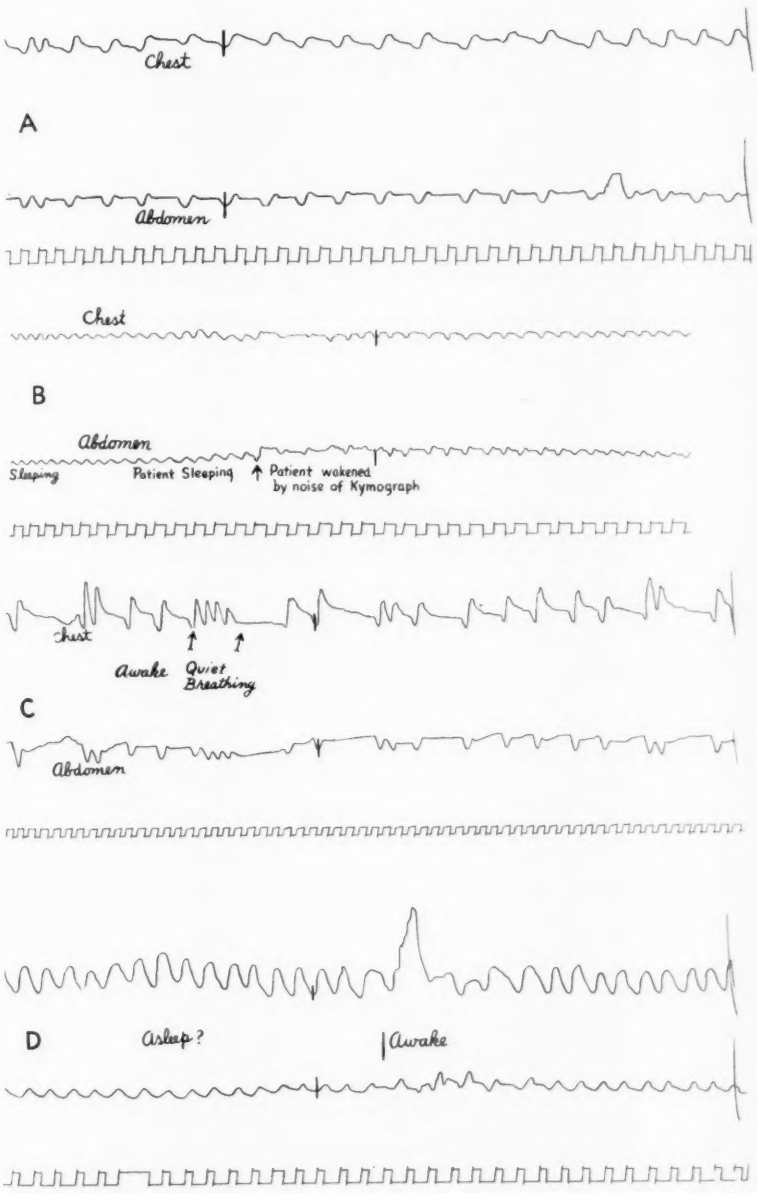

Fig. 4.—Tracings from patients with lobar pneumonia.

Figure 6 (tracings from pa in cases 3 and 4, table 4) shows examples of curves for patients with abdominal trauma. Figure 6 *A* is a tracing from a patient with fracture of the ilium with hematoma and with abdominal pain and tenderness, and figure 6 *B*, from a patient

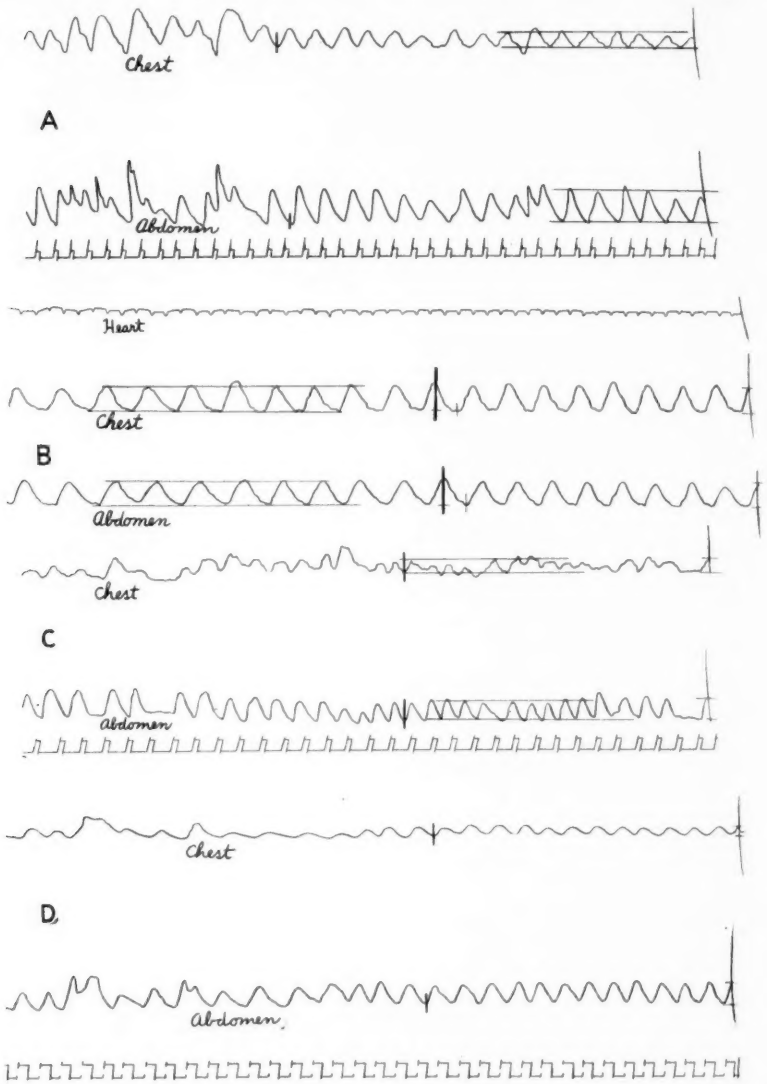

Fig. 5.—Tracings from patients: *A*, case 1, table 3; *B*, case 2, table 3; *C*, case 3, table 3; *D*, case 6, table 3.

with traumatic rupture of the kidney. Both of these show marked restriction of the abdominal respiratory excursion with a free thoracic excursion.

In figures 7 and 8 the heights of the curves from the thoracic and abdominal respiratory movements are represented diagrammatically. The diagonally marked columns represent the thoracic movements and the solid black columns the abdominal movements. The paired arrangement represents these two for the same respiration.

In figure 7 are represented the respiratory excursions in ten hospital patients of various ages, whose diagnoses are listed in table 1 and who were selected to represent the normal. In figure 8 is a larger series from patients admitted to the hospital for tonsillectomy and chosen as normal controls. It appears from the tracings for these two groups

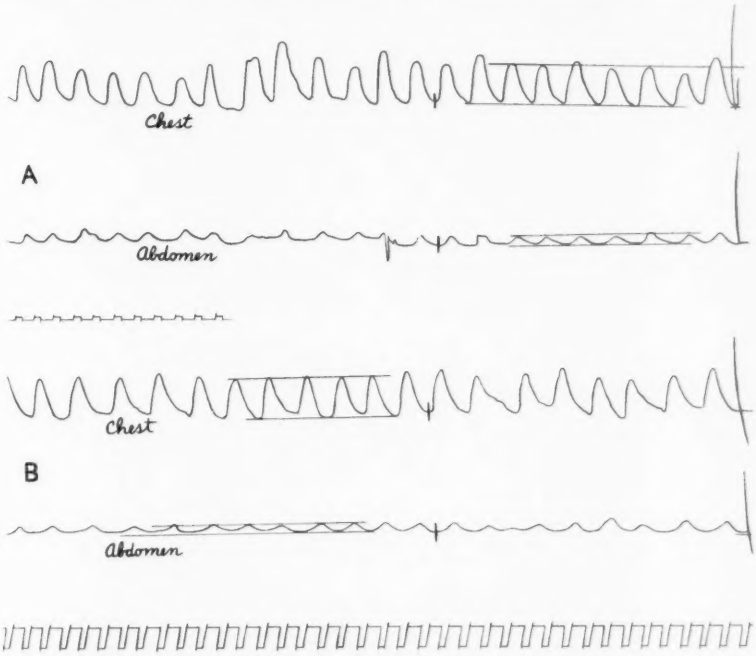

Fig. 6.—Tracings from patients: *A*, case 3, table 4; *B*, case 4, table 4.

that under normal conditions the abdominal respiratory excursion in children is usually but not invariably greater than the thoracic excursion, the abdominal excursion being greater in nine of the ten cases in the first group and in twenty-two of the twenty-four cases in the second group.

Also in figure 7 the first group of columns represents the respiratory excursions in sixty-nine patients that were subsequently operated on for appendicitis or abscess arising from appendicitis. In sixty-five of the cases the diagnosis of an inflammatory condition involving the appendix was confirmed at operation. In the other cases (11, 12, 17

and 21), while the appendix was not isolated at operation, the diagnoses, listed in table 2, were also not in doubt. In all of the sixty-nine cases excepting these four and 5, 8 and 27, in which the appendix was not examined histologically, the diagnosis of acute appendicitis was further confirmed by laboratory examination.

Of the sixty-nine cases of appendicitis, the abdominal respiratory excursion was less than the thoracic excursion in fifty-five, equal to it

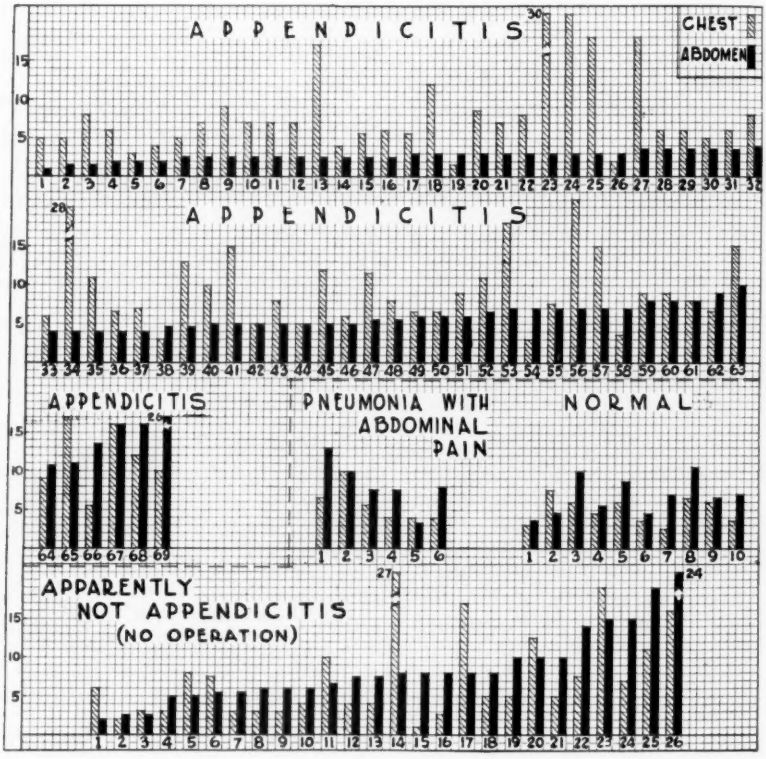

Fig. 7.—Diagrammatic representation of heights of curves from thoracic and abdominal respiratory movements.

in four, and greater than it in ten, making a percentage of 79.7 in which there was restriction of the abdominal excursion as compared with the thoracic excursion.

The cases of appendicitis in figure 7 are arranged in order of the degree of abdominal restriction. In table 2 they are listed in the order in which they appear from left to right in figure 7 and are classified as instances of acute appendicitis, acute appendicitis with local peritonitis, acute appendicitis with general peritonitis and acute appendicitis with abscess. In cases in which perforation of the appendix was found

that also is noted. In addition, the age of the child is given, and in the column to the right it is indicated whether the abdominal respiratory excursion was less or greater than the thoracic excursion.

In about one half of the cases classified as instances of acute appendicitis without complications there was noted some local peritoneal exudative reaction, usually of a fibrinoplastic type, limited to the appendix or the immediately adjacent parts and showing perhaps a little free serous fluid. A very small amount of frank pus was noted in one case.

When the local peritoneal reaction involved more than just the appendix and contiguous tissues but was limited to the lower portion of the abdomen the condition was classified as acute appendicitis with local peritonitis. The exudate was usually purulent.

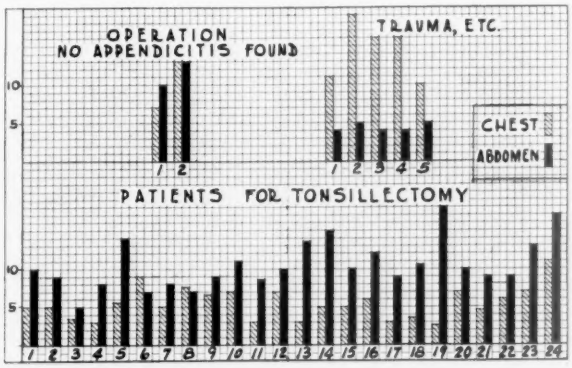

Fig. 8.—Diagrammatic representation of heights of curves from thoracic and abdominal respiratory movements.

When the peritoneal cavity was involved more or less as a whole, with a purulent or fibrinopurulent reaction, the phrase acute appendicitis with general peritonitis was applied.

The expression acute appendicitis with abscess indicates that there was an accumulation or pocket of pus limited to the region of the appendix.

An analysis of the fourteen cases which were exceptions to the rule that the abdominal respiratory excursion is less than the thoracic excursion in acute appendicitis failed to elicit adequate explanation for these exceptions. The lungs seemed to be normal in each of these instances. The respiration was "shallow" in case 66. In case 38 the breathing was described as "grunting" and "shallow," as if from "pain," but the lungs were found to be clear. The thoracic respiration was said to be "guarded" in case 61.

In figure 7 are also represented the respiratory excursions in six cases of pneumonia with abdominal pain and tenderness or rigidity of the sort that might suggest an acute inflammatory condition of the abdomen (table 3). It is to be noted that in only one of these cases (case 5) was the abdominal excursion less than the thoracic—quite contrary to the usual finding in acute appendicitis (figs. 2, 3 *A*, 3 *B* and 3 *D*).

Figure 7 also shows respiratory excursions in a series of cases in which there were abdominal symptoms but in which operation was not

TABLE 5.—*Abdominal Symptoms (No Operation)*

Case	Age		Diagnosis	Abdominal Symptoms	
	Yr.	Mo.		Pain*	Tenderness†
1	8		Acute gastro-enteritis	Yes	No
2	2	6	Pyelitis	Yes	Yes
3	3	4	Acute infection of upper respiratory tract	Yes	No
4	3	9	Osteomyelitis of left tibia, healing (also pulmonary or pleural condition ?)	‡	‡
5	8	9	Hysteria ?	Yes	No
6	7	9	Acute infection of respiratory tract	Yes	Yes
7	12		Scarlet fever	Yes	Yes
8	1	11	Fecal impaction	Yes	?
9	8	4	Pyelitis and probably pyelonephritis	‡	Yes
10	10	4	No diagnosis (pus in urine)	Yes	?
11	8	10	Infection of upper respiratory tract	Yes	Yes
12	12	3	Subacute appendicitis ?	Yes	Yes
13	11	10	No diagnosis	Yes	Yes
14	7	6	No diagnosis; appendicitis ?	Yes	Yes
15	10		Obstipation and intercostal neuralgia	Yes	‡
16	8	11	Scarlet fever	‡	‡
17	8	2	Chronic otitis media; appendicitis ?	Yes	Yes
18	6	9	Acute nasopharyngitis	Yes	Yes
19	8	8	Acute pharyngitis	Yes	Yes
20	7	11	Acute tonsillitis	‡	Yes
21	8	3	Intercostal neuralgia	Yes	Yes
22	12		Acute encephalitis ?	‡	Yes
23	11		Arthritis of right hip ?	Yes	No
24	11	8	Acute catarrhal jaundice	Yes	Yes
25	10		Acute pharyngitis	Yes	Yes
26	12	3	Acute pharyngitis	Yes	Yes

* Abdominal pain was noted at one time or another during the illness.
† Tenderness in many cases was not localized.
‡ Not recorded.

done, on the assumption that there was no appendicitis or other acute condition requiring operation. These cases, with diagnoses, are listed in table 5. It is quite possible that some of these may have been cases of mild or subsiding appendicitis. It is to be noted, however, that in seventeen of twenty-six, or 65.4 per cent, of these cases the abdominal respiratory movement was greater than the thoracic movement.

In figure 8 (table 6) are shown the respiratory movements in two cases in which the diagnosis of appendicitis was followed by operation, with the finding of an apparently normal appendix. In the first case

the abdominal excursion was greater than the thoracic, and in the second the excursions were equal and unusually full. These proved on operation to be cases of mesenteric lymphadenitis.

In figure 8 (table 4) are represented five cases of acute abdominal conditions, with tenderness or tenderness and rigidity, not due to appendicitis but including cases of trauma. In these there were free thoracic respiratory excursions with definitely restricted abdominal excursions in every instance, thus illustrating the fact that conditions in the abdomen other than acute appendicitis may cause restriction of the abdominal respiratory movement.

TABLE 6.—*Operation—No Appendicitis Found*

Case	Age Yr.	Age Mo.	Diagnosis	Abdominal Symptoms
1	10	9	Infection of upper respiratory tract and enlarged mesenteric lymph glands	Pain and tenderness
2	11		Mesenteric lymphadenitis.....	Pain and moderate tenderness

SUMMARY AND CONCLUSIONS

The abdominal and thoracic respiratory movements of children were registered simultaneously on smoked drums, and the heights of the curves from these two regions were compared, with the following results:

1. In fifty-five, or 79.7 per cent, of sixty-nine definite cases of acute appendicitis the excursion of the curve produced by the abdominal movement was less than that of the thoracic movement. (In the normal child the amplitude of the abdominal curve is usually greater.)

2. Restriction of the excursion of the abdominal movement, as might be anticipated, was also found in some other acute abdominal conditions that caused tenderness or tenderness and rigidity of the abdominal wall, as illustrated by one case each of nephrolithiasis, pneumococcic peritonitis, fracture of the ilium with hematoma, traumatic rupture of the kidney and traumatic rupture of the left adrenal with peritoneal hematoma.

3. On the other hand, restriction of the respiratory abdominal movement was absent in all but one instance in six cases of pneumonia (five of lobar, one of postoperative, type) in which abdominal tenderness, rigidity or both were present. (A larger series of such cases should be studied for proper evaluation of this finding.)

4. The abdominal curves were free and of full height in two cases of mesenteric lymphadenitis with abdominal pain and tenderness which were diagnosed as appendicitis preoperatively.

In view of these findings I consider that restriction of the abdominal respiratory movement, as indicated by the pneumographic tracing, when considered in connection with the other usual symptoms and signs of appendicitis is a frequent and valuable, though not a constant, sign in acute appendicitis in children of the ages studied.

Dr. C. J. Eldridge, now of Kansas City, Mo., collaborated in the early part of this study during the period of adaptation of the recording apparatus and making of the first tracings in patients with appendicitis. Acknowledgment also is due to various other members of the resident staff for help in collecting the tracings in cases of acute appendicitis.

THE RATIONAL TREATMENT OF ABNORMAL LABIAL FRENUM

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The treatment of abnormal labial frenum is often a matter of dispute. The oral surgeon, rightly enthusiastic over his prowess in fashioning normal structures out of marred oral tissues, is apt to advise excision. The pediatrist, witnessing the remarkable mending of abnormal structure and function in the process of growth, is inclined to advise leaving the affected structure alone.

While dental texts reflect a lack of decisive thought on the subject, a questionnaire conducted by the *International Journal of Orthodontia and Dentistry for Children*[1] reveals a growing skepticism among orthodontists regarding the advisability of excision. Leaders in this field are of the opinion that in most instances a thickened labial frenum will correct itself with the coming of the permanent canines and the second and third molars.

Confused parents often turn to the pediatrist to help decide what constitutes an abnormal frenum and how such abnormality should be corrected.

The normal frenum is a band of tissue that connects the inner surface of the lip to the corresponding gum. The upper frenum (frenulum labii superioris) is the better developed and may be brought into view by everting the upper lip. The attachment of this frenum to the lip begins about a centimeter below the vermilion border and ends a few millimeters above the interdental papilla of the central incisors. The diverging fibers of the frenum are frequently seen passing over the gingival crest to end in the palatal tuft on the lingual side of the gum margin.

Inspection of numerous normal infants in office practice has revealed that a so-called abnormal frenum is exceedingly common in infancy. In the 1 year old infant the frenum frequently exhibits an exaggerated thickening as it passes over the gingival crest between the central incisors, and this thickening appears to constitute a barrier to normal approximation of the incisors (fig. 1 *a*). In children of this age a

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1. Internat. J. Orthodontia **19**:448, 1933.

space between the incisors is more often present than not, and this condition in the infant does not presage the existence of a thickened frenum in the older child. As the child grows older the alveolar process grows downward as well as forward, and the attachment of the frenum is found farther away from the interdental papilla (fig. 1 *B*).

In a survey made of the mouths of children in two separate schools [2] the degree of spacing between the incisors and the position of the frenum were recorded. Of 116 children varying in age from 3 to 6 years, inclusive, 26 had sufficient thickening of the frenum with low attachment to be designated as abnormal. Of these, 15 had separation of the upper central incisors. In 11 other children with thickened frenums the incisors were absent. Among 128 children from the third to the seventh grade—pupils aged 9 to 13 years, inclusive—only 8 had abnormal frenums, 4 with separation of the incisors. In the 13 year old group alone there were 62 children, 3 of whom had abnormal frenums, 1 with separation of incisors.

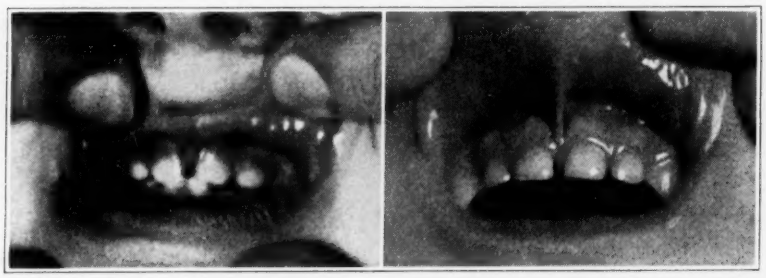

Fig. 1.—*A*, K. B., aged 1 year, showing the thickening of the frenum common at this age. *B*, same child, aged 3½ years, showing less thickening of the frenum and higher attachment with increasing age.

From these figures the conclusion seems warranted that as the child grows older the attachment of the frenum is found farther away from the gingival crest (fig. 2), and the presence of separation of the incisors is less frequent.

Determination of a thickened frenum as an etiologic factor in malocclusion should therefore not be made too early. The eruption of the permanent incisors may eliminate an apparent thickening of the frenum (fig. 3).

If the abnormal frenum persists after the eruption of the permanent incisors and canines it would seem reasonable to attempt correction of separation of the incisors by the use of appliances rather than by surgical intervention.

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2. Normal School (State Teachers' College), Milwaukee, and Richards School, Whitefish Bay (Milwaukee).

The correction of abnormal spacing between the incisors by means of mechanical appliances rather than by excision seems not only logical but in accord with the embryologic nature of this abnormality. Bolk [3] in a careful study of the embryology of the structures of the mouth demonstrated that in the development of the vestibulum oris the frenum is pushed up as an intermediate bridge. He pointed out that at one stage of development the upper lip is in reality divided into a right and a left lip—a situation also present in some of the adult lower primates.

Fig. 2.—K. W., aged 7 years, showing normal position of the frenum attachment after eruption of the permanent incisors.

Fig. 3.—*A*, C. M., aged 4 years, showing exaggerated thickening and abnormal attachment of the frenum with separation of deciduous incisors. *B*, same child, aged 6½ years, showing improvement after eruption of the permanent incisors.

A widening of the frenum, said Bolk, should be regarded not as a hypertrophy but as a developmental defect in which the fusion of the two sides of the vestibulum oris has not been completed. In persons with such a condition the tissue strip in which the teeth develop is equally incomplete. From this finding it would seem to follow that the indicated procedure is not excision of the frenum but such orthodontic measures as will bring the central incisors together. On embryologic

3. Bolk, L.: Ztschr. f. Morphol. u. Anthropol. **14**:241, 1912.

grounds excision of the frenum with its resultant scar tissue would seem definitely contraindicated, as it also seemed to be from our clinical observations.

Too early operative excision may produce scar tissue hindering the approximation of the incisors (figs. 4 and 5).

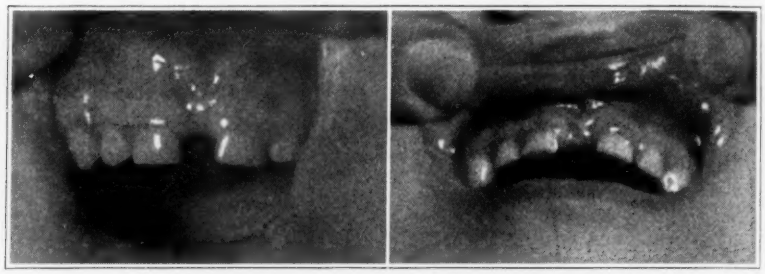

Fig. 4.—*A*, C. W., aged 4 years, showing wide spacing of the incisors and scar tissue following excision of the frenum. The frenum was excised in the summer of 1932; the photograph was taken on March 18, 1933. *B*, same child, aged 6 years, showing spacing between the incisors unimproved despite excision of the frenum. Scar tissue is more pronounced.

Fig. 5.—M. K., aged 7 years, showing spacing of the incisors and excessive scar tissue after excision of the frenum. The photograph was taken two years after excision.

CONCLUSIONS

1. Thickening of the superior labial frenum is common in infancy.

2. This thickening of the frenum becomes less noticeable as the child grows older.

3. There is insufficient evidence that the abnormal frenum has any relation in the majority of instances to separation of the upper incisors or to malocclusion.

4. Separated central incisors are more easily moved together by appliances before than after scar tissue is formed.

5. The eruption of the full complement of permanent teeth will often correct separation of incisors and abnormally thickened frenum.

PATHOGENESIS AND TREATMENT OF MYOTONIA CONGENITA

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Myotonia congenita is a disease of the muscles characterized by slowness of relaxation after voluntary contraction. It is manifested clinically by tonic cramps and muscular hypertrophy. The hereditary nature and the detailed clinical picture of the disorder were first clearly elucidated, in 1876, by Thomsen, in whose family the disease had existed for five generations. Myotonia had previously been described as a symptom by Bell and Benedict, but the first authentic account of the disease was published by Leyden in 1874.[1] Thomsen's [2] report of 23 cases (including his own) in his own family stimulated a great deal of interest. At the suggestion of Bartels, a clinician in Kiel to whom Thomsen had submitted his manuscript, the title of his report was changed from "Ataxia Muscularis" to "Tonic Cramps in the Voluntary Muscles in Consequence of an Inherited Psychical Disposition." This title was selected because, in Bartel's opinion, the psychic element and the hereditary predisposition were the two dominating and most interesting aspects of the disorder.

Subsequently, other reports of cases and other ideas as to the pathogenesis of the disease were added to the literature. In 1881 Strümpell [3] reported a case of the typical form and placed the condition in the category of a primary myopathy. He felt that it was a distinct clinical syndrome characterized by a congenital anomaly of the muscular system for which no anatomic cause could be demonstrated. Because of its congenital myopathic nature he proposed the shorter and more descriptive term myotonia congenita.

From the Department of Peditarics of the University of Illinois College of Medicine.

1. Nissen, K.: Beiträge zur Kenntnis der Thomsenschen Krankheit (Myotonia congenita) mit besonderer Berücksichtigung des hereditären Momentes und seinen Beziehungen zu den Mendelschen Vererbungsregeln, Ztschr. f. klin. Med. **97**:58, 1923.

2. Thomsen, J.: Tonische Krämpfe in willkürlich beweglichen Muskeln in Folge von ererbter psychischer Disposition (Ataxia muscularis), Arch. f. Psychiat. **6**:706, 1875.

3. Strümpell, A.: Tonische Krämpfe in willkürlich bewegten Muskeln (Myotonia congenita), Berl. klin. Wchnschr. **18**:119, 1881.

The first systematic attempt to study the pathogenesis of this disease appeared four years later, with the monographic work of Erb.[4] Erb collected reports of twenty-eight cases of the typical form and divided the patients showing myotonia as a symptom into three classes: (1) those with typical myotonia congenita; (2) those with dubious forms which do not agree in every important point but show a great similarity to myotonia congenita, and (3) those with myotonia associated with disease of the nervous system.

He described an increased irritability of the muscles in response to mechanical, galvanic and faradic excitation, which he believed to be characteristic of myotonic muscle, and designated it the myotonic reaction. He also described positive histopathologic changes in the muscles of his patients, as shown by biopsies, and thus recorded the first definite morphologic observations concerning the disorder. (Previous to Erb's report biopsy specimens from patients with myotonia congenita were reported as normal.) Other investigators subsequently confirmed Erb's observations, with insignificant additions or subtractions. The morphologic factors in most cases were multiplication of sarcolemic nuclei, hypertrophy of the muscle fibers and dissociation of the sarcous elements. Déjerine and Sottas[5] maintained, however, that the histopathologic features described were the result and not the cause of the disease. They based their opinion on a thorough postmortem study of a patient with myotonia congenita who had died from uremia following acute nephritis. The report was not well received generally as many writers claimed that the tissues examined by Déjerine and Sottas were obscured by serous infiltration incident to the renal insufficiency.

With regard to microscopic changes in the muscles, there was little unanimity of opinion among the various workers and, peculiarly enough, even on the part of the individual investigator. This is illustrated by the two reports of Jacoby.[6] In his first communication[6a] he described changes in the muscles similar to those reported by Erb. Eleven years later,[6b] however, when he reported his second case he maintained that most of the changes previously described by himself and other investigators were artefacts. Not only did Jacoby's report reflect his scientific sincerity, but that report and the conflicting opinions of other writers suggested the lack of reliable data favoring morphologic alteration of the muscle as a primary factor in myotonia congenita. Subsequently other theories as to the pathogenesis were propounded. Since most of

4. Erb, W.: Die Thomsen'sche Krankheit (Myotonia congenita), Leipzig, F. C. W. Vogel, 1886.

5. Déjerine, J., and Sottas, J.: Sur un cas de maladie de Thomsen suivi d'autopsie, Rev. de méd., Paris **15**:241, 1895.

6. Jacoby, G. W.: (*a*) Thomsen's Disease (Myotonia Congenita), J. Nerv. & Ment. Dis. **14**:129, 1887; (*b*) On Myotonia, ibid. **25**:508, 1898.

them were not supported by adequate clinical observations under controlled conditions or by experimental observations, they may be designated briefly by the terms psychopathic, neuropathic, myopathic, chemical-toxic and endocrine. They were, for the most part, attempts at hypothetic explanations of the pathogenesis on the basis of the observation of cases or of abstract thinking. The details of these conceptions are reviewed by Steiner [7] and Nissen.[1]

The various theories were subjected to scientific scrutiny with the more general use of experimental methods in medicine at the start of the twentieth century. Many of the investigators had abandoned psychogenic and neuropathic influences as primary pathogenic factors because they were not in complete harmony with the observations. The lack of authenticated structural changes revealed on biopsy in the muscles of patients with typical myotonia congenita suggested the possibility of primary physicochemical change. Since the chemistry of the muscles was poorly understood, the mechanism was first conceived as a peculiar disorder of metabolism which was expressed locally in the muscles as myotonia. One of the first investigations to be cited in confirmation of this hypothesis was that of Ringer.[8] Ringer found that perfusion of a frog's curarized muscle with sodium phosphate and sodium bicarbonate resulted in prolonged contraction and spastic rigidity following faradic stimulations.

Similar findings were noted by other observers in the poisoning of muscle with veratrine, and later the myotonic reaction was produced experimentally with other substances, some of which were not inherently poisonous.[9] This led to a modification of the physicochemical theory, in that the fault in muscular metabolism was ascribed to an increase in the catabolic processes and a delay in removal of waste products. Jensen [10] was one of the first to carry out a well prosecuted clinical investigation along these lines. Myographic curves for patients with myotonia congenita had been recorded by investigators before Jensen, but essentially such curves were a graphic confirmation of what one could have noted by direct observation. His contribution was to analyze the phenomena of the myotonic muscles, as recorded in the myographic curves, and to attempt to deduce the vital processes responsible for such behavior of the muscles. On comparing the data from myotonic and normal sub-

7. Steiner, W. R.: Thomsen's Disaese (Myotonia Congenita), in Osler, W., and McCrae, T.: Modern Medicine, Philadelphia, Lea Brothers & Co., 1909, vol. 6, p. 595.

8. Ringer, S.: Report on the Influence of Rhombic Sodium Phosphate and Sodium Carbonate on Muscular Contraction, Brit. M. J. **2**:114, 1884.

9. Pansini, S.: Sulla malattia di Thomsen (myotonia congenita), Naples, V. Pasquale, 1907; abstr., Semaine méd. **28**:175 (April) 1908.

10. Jensen, P.: Zur Analyse der Muskelstörung bei der Thomsen'schen Krankhheit, Deutsches Arch. f. klin. Med. **77**:246, 1903.

jects, Jensen observed that the defect was due mainly to retardation of the relaxation process. Accordingly, he reasoned that there was an abnormal delay in the process of assimilation of substances which carry the muscle back to the original working condition, as well as a possible defective process of elimination of the products of catabolism. To prove his contention he studied the effect of heat on the myotonic muscle and found that the muscular contraction approached normal. Since heat improved the assimilation process, he felt he had established his premise. He next investigated orchic and thyroid extracts on the assumption that such substances create metabolic heat and might therefore affect the muscular tissue in the same manner. After injecting crude extracts of these glands he found only a transient effect, but he suggested that other therapeutic experiments be tried along the line suggested, as the substance of the muscles itself appeared to be the seat of the disturbance. For some reason or other, this study did not receive the subsequent attention from other investigators that it seemed to merit, nor did Jensen himself extend his preliminary observations.

Another important contribution to the subject was Pansini's monographic treatise [9] on myotonia congenita published in 1907. The book includes a very complete discussion of the subject and the literature to that time. Pansini administered thyroid to one of his patients with questionable success but found that epinephrine made his patient definitely worse. He was of the opinion that the dysfunction in myotonia congenita lay solely in the muscle and did not involve the nerve. In discussing the pathogenesis he said: "The chief reason for the variable state of myotonia comes most probably from the variation in the blood of the quantity of the secretion of the internal glands. It is also probable that these substances which have the capacity to excite or diminish the myotonic state may not act specifically." Other experiments were carried out sporadically by numerous workers in an attempt to test the hypothesis of defective muscular metabolism but were limited always by the lack of fundamental facts concerning the chemistry and physiology of muscular tissue. After the relationship of creatine and creatinine excretion to degenerative and hyperplastic states present in muscle had been demonstrated, Findlay [11] investigated the relationship of these findings to myotonia congenita. In a study of the case of a young man with myotonia congenita Findlay found no excretion of creatine with a creatine-free diet and a high normal or slightly elevated creatinine coefficient. Accordingly, he argued that not only was the evidence against degenerative changes in the muscles but the high creatinine coefficient might be indicative of increased muscular efficiency

11. Findlay, L.: A Case of Thomsen's Disease, Quart. J. Med. **5**:495 (July) 1912.

engendered by excessive effort to overcome spasm. He considered the disease not as primarily or wholly a disorder of the muscles but as one involving the nervous system as well.

Two years later Rosenbloom and Cohoe [12] undertook a more complete metabolic study of a man with myotonia. As did Findlay, they found that no creatine was excreted in the urine when the subject was on a creatine-free diet and that the creatinine coefficient was within the upper limits of normal. Their patient manifested a negative calcium balance, and they attempted to show that loss of calcium may play a part in producing the symptoms of myotonia congenita.

In 1924 Nissen,[1] a grandnephew of Thomsen, completed the genealogical survey of the disease in their family through the seventh generation and exhaustively reviewed all the scientific data, except those in Pansini's monograph, which had accumulated since the first report of the disease. The omission of Pansini's data is unfortunate. His conclusions concerning the nature of Thomsen's disease were as follows: (1) Myotonia congenita (Thomsen's disease) should be classed with the myopathies; (2) its hereditary aspect should be regarded as established; (3) the immediate cause of the myotonia should be sought in a change in the sarcoplasm brought about by physicochemical changes in the germ plasm; (4) the prognosis is absolutely favorable for life but is unfavorable for the myotonia, and (5) every form of therapy has been without lasting effect.

In the final paragraph of his discussion he stated:

> We shall be unable to progress in the explanation of Thomsen's disease without postmortem examination and we must seek as our goal the chance to make a thorough dissection of the entire central nervous system, the medulla and the peripheral nerves, with their terminal plates, of a myotonic patient

Thus, despite some promising experimental and clinical observations, the etiology and pathogenesis of myotonia congenita appeared to be just as obscure and in just as controversial a state as they were in the latter part of the nineteenth century. At each critical point, when promising leads seemed established, the line of thought was not properly extended because of a lack of knowledge of fundamental facts. Within the past few years there have been some definite advances in the chemistry of muscle,[13] which throw some light on the possible mechanism of this disorder. For that reason the observations on the following case are recorded after three years of study.

12. Rosenbloom, J., and Cohoe, B. A.: Clinical and Metabolism Studies in a Case of Myotonia Congenita: Thomsen's Disease, Arch. Int. Med. **14**:263 (Aug.) 1914.

13. Eggleton, P.: The Chemistry of Muscle, in Luck, J. M.: Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1935, vol. 4, p. 413.

REPORT OF A CASE

F. H., a white boy, aged 5 months, was admitted to the pediatric service because he was suffering from generalized tonic spasms and cyanosis. Dr. J. H. Hess gave us the opportunity to study the case. The history showed a normal birth, but the hospital records carried a notation that the infant appeared "chesty." At birth his weight was 7 pounds (3,175 Gm.) and his length 49 cm.

The only evidence of a pathologic condition in the period immediately after his birth was that, according to the mother, his tongue seemed large and protruded from his mouth, which made it difficult for him to nurse well at the breast. When he was 5 weeks old the mother's secretion of milk decreased to the point where it failed to satisfy him. It was at this time that she noted that he became cyanotic and rigid after crying. Despite the institution of artificial feeding, the attacks increased in severity and frequency until there were days when the infant was free from attacks for only from ten to fifteen minutes. At the age of 6 weeks he was given calcium gluconate, and the mother was of the opinion that this decreased the number of attacks for a short time. When the infant was 8 weeks of age, a diagnosis of enlargement of the thymus was made, and he was given four roentgen treatments within a period of five weeks. After the first treatment the attacks became unusually severe, but they were relieved somewhat by the administration of elixir of phenobarbital in 1 drachm (4 cc.) doses every four hours. After the third roentgen treatment the infant contracted bronchitis with fever, and the attacks again became severe. Parathyroid extract was given without any beneficial effect. The number of attacks now varied between twenty-five and thirty daily, and the "chesty" appearance noted at birth was becoming more marked. Definite enlargement of the muscles of the arms, legs and back was evident. The mother's description of the typical attack was as follows: "The child cries, and his tongue protrudes and changes from flat and flabby to pointed and tightly contracted. His eyes shut so tightly that they look puffy, and his cheeks become prominent. His mouth remains wide open, but he becomes unable to make a sound. His arms extend, with fists tightly closed, and the muscles all over the body seem prominent. His legs become so stiff that they cross. The entire skin surface becomes white, then red and finally blue, and he appears to be holding his breath. Within a few minutes his muscles relax, and his color returns." The attacks seemed to be precipitated by cold, by fright, on waking or at the beginning of feeding when he started to suck.

Past History.—Delivery, after labor lasting four hours, was normal and spontaneous. Presentation was cephalic. The child's condition at birth was good. When 5 months of age he had no teeth. He was then unable to sit up, but he noticed his father and mother.

For five weeks he was breast fed, and since then he had been given a cow's milk and sugar formula suited to his age. At the age of 3 months he was given orange juice for one week only. When he was 2 months old the giving of cod liver oil, 40 drops daily, was begun, and from the time he was 4 months old he had been given cereal twice daily. He received no vegetables but occasionally was given from 1 to 1½ ounces (28 to 42 Gm.) of carrot or spinach water.

Family History.—The mother, who was 23 years of age and in good health, was a native of Budapest, Hungary. She had had only the one pregnancy. The father was 26 years of age and in good health. He was born in the United States, of German ancestry. There was no history of myotonia congenita or of any

other disorder involving muscular function in the grandparents or others of their generation, on either side of the family.[14]

Physical Examination.—Physical examination revealed a well nourished, abnormally developed white boy 5 months of age, who did not appear acutely ill except during the attacks which will be described later. He had the general appearance of an infant Hercules, owing to the marked enlargement of the muscles all over his body. His tongue was large and thick, and it protruded most of the time. He seemed interested in his environment but lacked the spontaneity of movement an infant of his age usually shows. His weight was 4,700 Gm., his length, 56.5 cm. and his sitting height, 34 cm. The anterior fontanel measured 30 by 20 mm. The occipitofrontal circumference of the head was 38.8 cm., and the circumference of the neck was 24 cm. The circumference of the chest at the nipple line was 39 cm., and the circumference of the abdomen at the umbilicus, was 34.5 cm. The circumference of the midforearm was 11.6 cm., that of the midthigh 17 cm. and that of the midcalf, 12 cm.

The most conspicuous feature noted at physical examination was the marked hypertrophy of all the muscles of the body. On regional examination considerable sweating about the forehead was noted. The infant's hair was blond and of fine texture. He had a large tongue of normal color, which contracted readily when stimulated but did not show the myotonic reaction. There was enlargement of the muscles of the neck, and the thyroid was palpable but not enlarged. The thorax was well developed and showed uniform muscle hypertrophy. The abdominal muscles were firm and hypertrophic, but diastasis of the rectus muscles was present during the attacks. Umbilical hernia and bilateral inguinal hernia were present.

The extremities were characterized by an enormous overdevelopment of all muscles. They were unusually firm for an infant, and showed a localized dimpling and sustained contraction on mechanical percussion (fig. 1). The reflexes were normal. Typical attacks were provoked by any procedure which excited or caused discomfort to the patient and were continuous during the examination. During the attacks the patient became cyanotic, his eyes closed tightly, his mouth opened, his thighs were slightly flexed, his legs were hyperextended, his arms were slightly abducted and his forearms were slightly flexed. Respiration became gasping, inspiration became deeper and there was a whining cry or grunt during inspiration. The respiratory movements ceased momentarily, and cyanosis appeared. Relaxation then set in, and the normal skin color returned. The patient perspired freely, and the muscles of his extremities relaxed. At the height of

14. The absence of myotonia congenita in the patient's father and mother and in his maternal and paternal grandparents may throw some doubt on the correctness of the diagnosis. What is known of the mendelian mechanism of inheritance should make one extremely cautious about inferring that the condition is not hereditary because no record of the defect can be found in the patient's ancestors. When there is little knowledge of the patient's family tree, such a presumption is patently unwarrented. There is but one inference properly to be drawn from the absence of myotonia in the past two generations of the patient's family—that the condition is not solely the result of a simple mendelian dominant, unmodified by other factors, genetic or environmental. Therefore, in the absence of more extensive knowledge of the child's heredity than is available, there is inadequate reason to raise a presumption against the hereditary explanation for myotonia in the patient. The reader is referred to Nissen's article [1] for a detailed discussion of the hereditary aspect of Thomsen's disease.

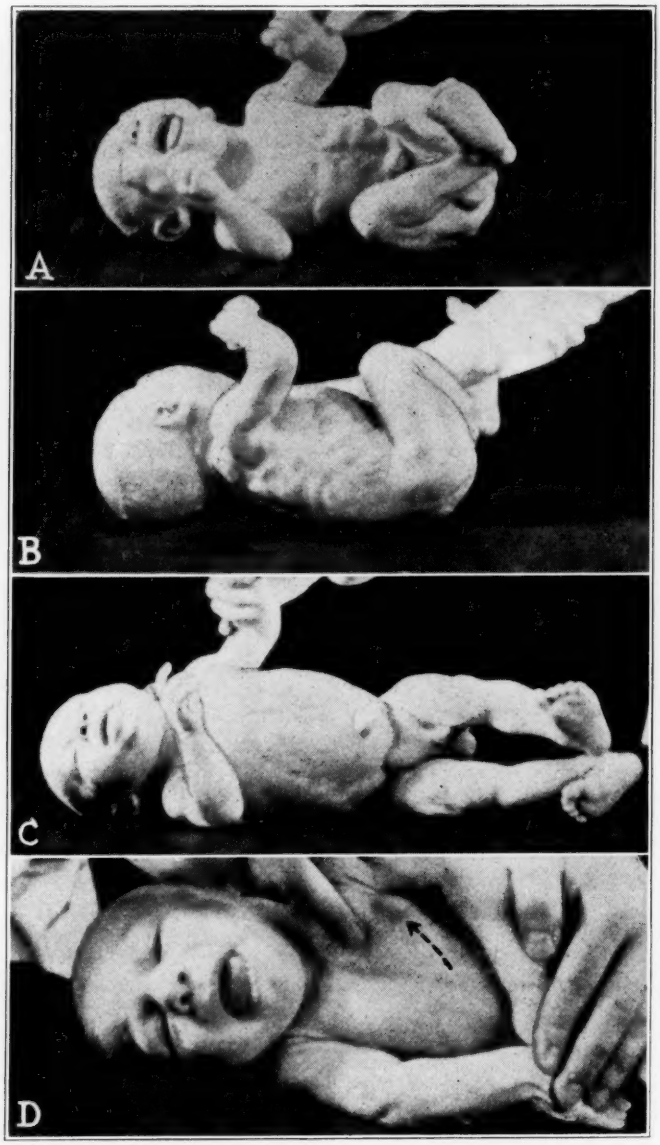

Fig. 1.—These photographs were made from a motion picture of the patient (F. H.), taken at the age of 6 months. The attack was precipitated by crying. In *A* the large tongue and the muscles of the face and the abdomen are shown in myotonic spasm. In *B* the muscles of the shoulder girdle and the back are shown in myotonic spasm. In *C* the spastic extension and adduction of the lower extremities, the umbilical and bilateral inguinal and scrotal hernias produced by increased intra-abdominal tension and the myotonia of the levator palpebrae superioris are shown. In *D* the arrow indicates the myotonic reaction of the pectoralis major produced by mechanical percussion.

the attack there was also evidence of increased intra-abdominal pressure, as the umbilicus protruded, and the inguinal hernias first became prominent and then descended into the scrotal sac. An entire attack lasted for from sixty to seventy-five seconds.

Special Examination.—When the patient was quiet, fluoroscopic examination gave negative results, but when an attack was provoked there was immediate cessation of movement of the left dome of the diaphragm, which was quickly followed by cessation of movement of the right dome. Both sides of the diaphragm remained fixed in the position assumed during deep inspiration until the attack subsided. At the beginning of relaxation the diaphragmatic movements were shallow, and then they gradually became deeper until respiration was normal.

The response of the muscles to galvanic stimulation was determined by testing the muscles of the forearm. The results were as follows:

5/5/33	Control (Normal Infant, Aged 6 Months)	Patient
Cathodal closure contraction.....	1.9	1.2
Anodal closure contraction.....	2.3	1.2

Neither the anodal nor the cathodal opening contraction was elicited in either child.

5/8/33	Control (Normal Infant, Aged 4 Months)	Patient
Cathodal closure contraction.....	2.0	2.2
Anodal closure contraction.....	2.4	2.1

Normally, galvanic irritation induces a single quick, short contraction on the making (closing) and, if the current be strong enough, on the breaking (opening) of the current. The contractions are most easily elicited on closing the current when the cathode is used as the active electrode (cathodal closure contraction). The normal response of the muscles to galvanic stimulation is represented by the following formula: CCC.> ACC.> AOC.> COC. In the patient, as the figures recorded show, the formula was at one time reversed (CCC. < ACC.) and at another altered so that CCC. = ACC. In addition, the galvanic stimulation resulted in a slow, wormlike contraction, which persisted for almost a minute after the stimulus ceased.

Roentgen examination of the long bones showed normal epiphysial development.

Direct laryngoscopic examination during an attack showed that the false cords appeared hypertrophic and that they almost met in the median line.

Chemical examination of the blood showed calcium 10.5 mg., potassium 28.3 mg. and phosphorus 6.1 mg. per hundred cubic centimeters of serum, and cholesterol 172 mg., dextrose 83 mg. and nonprotein nitrogen 34 mg. per hundred cubic centimeters of whole blood. The results of the Wassermann and the Kahn tests were negative. The blood count showed hemoglobin content 11.2 Gm. per hundred cubic centimeters (Newcomer), erythrocytes 4,590,000 and leukocytes 11,450. The differential count revealed polymorphonuclear neutrophils 64 per cent, lymphocytes 31 per cent, monocytes 3.5 per cent, eosinophils 1 per cent and basophils 0.5 per cent.

Biopsy of the gastrocnemius muscle was done, and the size and fibrillar structure of the muscle appeared normal.

Clinical Course.—In view of recent contributions to the literature on the function of creatine in muscle metabolism, it was of considerable interest to study the creatine-creatinine metabolism in this case. Only three investigators [15] had studied the creatine-creatinine metabolism in myotonia congenita (Thomsen's disease), and in both cases which they reported the subject was a man. Since creatine is not excreted in the urine of a male adult on a creatine-free diet (except under certain pathologic conditions, such as muscular atrophy, starvation and hyperthyroidism) the absence of creatinuria, as such, is not significant, whereas during the period of infancy and childhood, in which creatinuria is physiologic, its absence indicates an abnormal condition.

Accordingly, the patient was put on a creatine-free diet and placed on a metabolism frame. Twenty-four specimens of urine were collected, and tests for the preformed and the total creatinine were made in duplicate. The preformed creatinine was determined by the Folin colorimetric method,[16] and the total cre-

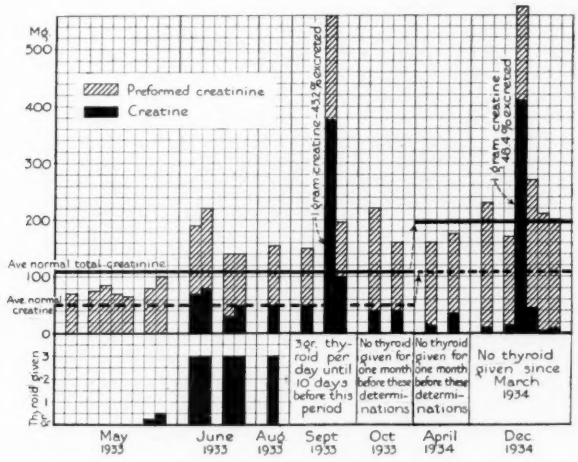

Fig. 2.—Chart showing the excretion of creatine and creatinine in twenty-four hour specimens of urine collected from the patient (F. H.) from 6 months to 2 years of age. The study was made during hospitalization.

atinine, by the autoclave procedure of Benedict and Myers.[17] At the start of the investigation it was not possible to keep the infant on the metabolism frame continuously because of the severity of the myotonia and on account of attacks of infection of the upper respiratory tract. The intermittent, complete twenty-four hour specimens of urine, however, showed, rather surprisingly, an absence of the physiologic creatinuria of childhood (fig. 2).

In a study of the creatine-creatinine metabolism in children with hypothyroidism we had corroborated the earlier finding of absence of the physiologic creatinuria and its restoration on treatment with thyroid.[18] Although there was only

15. Findlay.[11] Rosenbloom and Cohoe.[12]

16. Folin, O.: Beiträge zur Chemie des Kreatinins und Kreatins im Harne, Ztschr. f. physiol. Chem. **41**:223, 1904.

17. Benedict, F. G., and Meyers, V. C.: The Determination of Creatine and Creatinine, Am. J. Physiol. **18**:397, 1907.

18. Poncher, H. G.; Visscher, M. B., and Woodward, H.: Creatine Metabolism in Children with Hypothyroidism. J. A. M. A. **102**:1132 (April 7) 1934.

questionable evidence of a deficiency of thyroid in the patient whose case is here reported, it was decided to see what effect the administration of thyroid would have on him. The giving of thyroid was begun on May 12, 1933, in doses of ¼ grain daily, and was increased later to ½ grain twice a day. The dose was further increased gradually, and the myotonic symptoms proportionately abated, until on June 13 the patient for the first time since he was 5 weeks of age was free from symptoms and was excreting a normal amount of creatine for his age. Then the daily dose of 3 grains (0.18 Gm.) of thyroid was continued. In spite of the large doses of thyroid, the infant gained 2,000 Gm. in weight in a little more than two months. His muscles were no longer prominent, no myotonic reaction could be obtained from him and he seemed more alert. He was discharged from the hospital on August 20, definitely improved, and the mother was advised to continue giving him 3 grains of thyroid daily at home.

Fig. 3.—Photograph of the patient (F. H.), aged 8 months, after he had been treated with thyroid for two months. The gain in weight and the loss of muscular hypertrophy are evident.

The patient was readmitted on September 11, for further study, to see if it was necessary to continue longer with the thyroid. On his readmittance to the hospital the administration of thyroid was stopped, and ten days later he was still free from symptoms and was excreting a normal amount of creatine on a creatine-free diet. On September 28 1 Gm. of creatine was administered by mouth to determine the infant's tolerance, and for the first time since he had been under treatment he had a typical attack with cyanosis. It was not possible to account for this attack on the basis of abnormal retention of exogenous creatine since the amount of ingested creatine excreted (43.2 per cent) could not be considered abnormal when compared with the amount excreted by a normal infant of the same age. As it was not possible to keep the infant on a metabolism frame more than twenty-four hours after the ingestion of creatine, we do not have any data on the subsequent elimination, but the patient had no recurrence of myotonia. He

was discharged from the hospital on Octboer 8, after having been without treatment for one month. Except for the one attack after the creatine tolerance test the patient had been free from symptoms.

Two days after his discharge, however, there was a classic attack with generalized myotonia and cyanosis, and the mother returned the infant to the hospital. On studying his excretion of creatine it was found that, while the total amount excreted in twenty-four hours was below normal, creatinuria was present. At this point it would have been desirable to let the child continue without the administration of thyroid and to see whether the creatinuria would diminish and myotonia would return, but the parents were not sympathetic with the scientific aspect of the matter. In order to pursue study of the child with their cooperation it was felt advisable to resume treatment with thyroid.

On October 13 the infant again was discharged from the hospital. At that time he was receiving ½ grain (0.03 Gm.) of thyroid daily, which was to be increased in a few days to ¾ grain (0.045 Gm.).

On March 7, 1934, with the parents' permission, treatment with thyroid was discontinued. The child showed no symptoms until April 2. At that time, while he was having an attack of bronchitis, his mother noticed that the muscles of his neck would sometimes become rigid and draw his head to one side. Creatine-creatinine determinations were made, and it was revealed that the child was excreting creatine, but that the amount was considerably below normal for his age. No thyroid was given, and the infant was observed weekly during the summer and fall of 1934. There were no generalized attacks of myotonia or cyanosis, but the muscles of the neck and the arms were occasionally myotonic. The muscles were firm periodically, and the mother volunteered the information that they also "got stiff" occasionally. No myotonic reaction could be elicited. On December 19 the patient again acquired generalized myotonia with cyanosis and was brought back to the hospital. Creatine-creatinine determinations were made and showed that the patient was still excreting a small amount of creatine but that it was distinctly below normal limits. A test for tolerance of creatine made at that time showed that 48.8 per cent of the ingested creatine was excreted—an amount approximating that noted in the earlier test. The patient was discharged from the hospital on December 31, and arrangements were made to have twenty-four hour specimens of urine collected at home and brought to the laboratory.

Because of the concern of the parents over the return of the myotonia, the administration of thyroid was again started, although the urine was not free from creatine. The initial dose of ¼ grain (0.015 Gm.) of thyroid daily was gradually increased to ½ grain because although the patient was free from symptoms the excretion of creatine remained low.

On Jan. 20, 1935, the dose of thyroid was increased to 1 grain daily. This increase was followed by intense myotonic spasms of the arms, the legs and the diaphragm. The excretion of creatine, which had risen on the last increase in the dose of thyroid, dropped low at that time. The dose of thyroid was reduced to ½ grain daily on January 25, since it was thought that the amount had been increased too rapidly. Although with this dose the patient's excretion of creatine remained low he had no myotonic symptoms until February 7, when stiffness of the arms developed after an injection of diphtheria toxoid. There was recurrence of symptoms on February 14, 15 and 16. On February 16 the dose was increased to ¾ grain daily, and there were no more symptoms until March 21 and 22, when there were transient attacks of myotonia involving the arms. The dose was then increased to 1 grain daily, and the child was symptom-free until an infection of the upper respiratory tract developed on April 2. On April 10 the excretion of

creatine dropped very low, but he did not show symptoms until April 16. The myotonic symptoms became increasingly severe, so on April 22 the dose of thyroid was increased to 1½ grains (0.09 Gm.). The excretion of creatine continued at a low level in spite of the increased dosage.

On April 29 the child presented the classic picture of the paroxysmal stage of pertussis. In retrospect, it seems probable that the disease was present two weeks earlier. The question arose as to whether the patient manifested myotonic symptoms because of the infection and in spite of the increased dosage of thyroid or because of his tolerance to thyroid as a result of the development of antihormones. With these possibilities in mind, we thought it advisable to discontinue the giving of thyroid on April 30. On the following days, while the infant was without medication, the myotonia became so severe and generalized that thyroid was again given, after which the myotonia abated within twenty-four hours. With a dose of 1½ grains daily, the patient had myotonia only after a severe paroxysm of

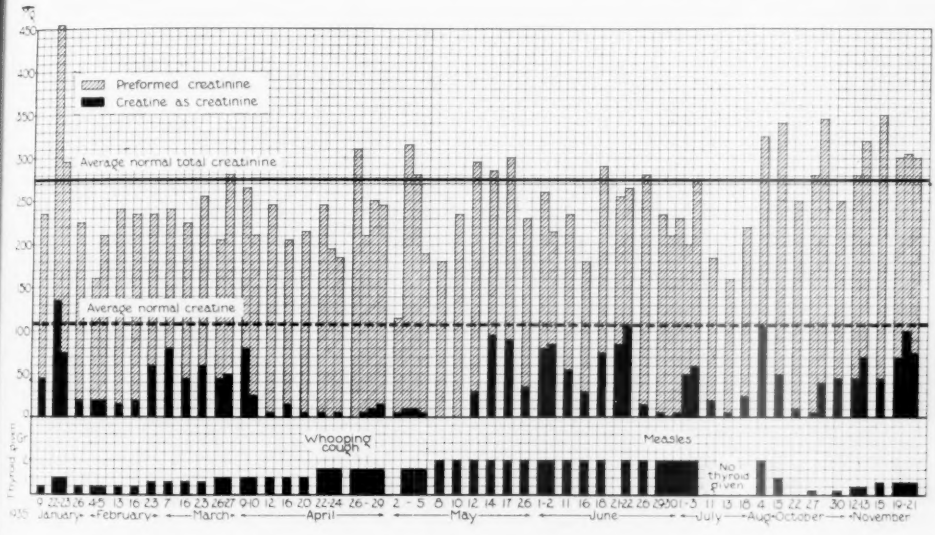

Fig. 4.—Chart showing the excretion of creatine and creatinine in twenty-four hour urine specimens collected from the patient (F. H.), from 2 to 3 years of age. Daily determinations were made from January 1 to July 20 and from October 22 to the end of the period covered by the report. Only those specimens which were complete were recorded here.

coughing. The amount was increased to 2 grains daily on May 6 but the excretion of creatine did not rise until May 11. At that time there was a noticeable absence of clinical symptoms, even during coughing, and a definite rise in the excretion of creatine. The patient continued to do well clinically and excreted an amount of creatine slightly below the normal level when he was given 2 grains of thyroid daily.

On June 21 the administration of thyroid was discontinued, but unfortunately the patient manifested fever and coryzal symptoms the next day, and the myotonia returned. Therefore, treatment with thyroid in doses of 2 grains daily was started again. Because the presence of measles was suspected, 7.5 cc. of convalescent measles serum was administered intramuscularly. This resulted in

definitely modifying the subsequent attack of measles, and, although the child's excretion of creatine was low, there was no myotonia. With convalescence from the measles and without further change in the dosage of thyroid, the excretion of creatine rose. The giving of thyroid was discontinued on July 9, because spontaneous improvement in patients with myotonia congenita during warm weather has often been reported in the literature. When the mother left for a vacation in the country she was instructed not to administer thyroid to the infant unless absolutely necessary. But on July 23, because the myotonic symptoms were returning, she resumed thyroid therapy, giving the former dose, of 2 grains daily. On their return to the city the patient was found to be free from symptoms and to be excreting a normal amount of creatine.

There was no change in the course of the disease until October 14, when the child's mother reported him to be very restless, perspiring freely and sleeping

Fig. 5.—Photograph of patient (F. H.), aged 3 years. At the time this picture was taken the myotonia had disappeared, and the muscular hypertrophy was no longer present. The following measurements were obtained: weight 15.8 Kg., length 93.75 cm., sitting height 57 cm., occipitofrontal circumference of the head 49 cm., circumference of the neck 28 cm., circumference of the chest 55 cm., circumference of the abdomen 50 cm., circumference of the midforearm 18 cm., circumference of the midthigh 31 cm. and circumference of the midcalf 22.5 cm.

poorly. The administration of thyroid was discontinued because it was felt that the patient was becoming intolerant to it, but within a week the excretion of creatine dropped, and myotonia appeared. It was then decided to give thyroid in very gradually increasing doses in order to determine the dose that would keep the patient free from myotonic symptoms without producing symptoms of hyperthyroidism. Starting with ¼ grain of thyroid daily, the dose had to be increased to ¾ grain to free the patient from the myotonic symptoms.

Further investigation with amino-acetic acid, thyroxin and other substances was then undertaken to determine the nature of the action of the thyroid and

to apply the results in arriving at the probable explanation of the pathogenesis of myotonia congenita. The details of that study will be reported later, but it may be stated here that, although amino-acetic acid induced creatinuria, it had no effect in relieving myotonic symptoms and that thyroxin was as effective as thyroid in equivalent doses.

COMMENT

The data obtained in the present study suggested a possible pathogenic relationship between the abnormal metabolism of creatine and the myotonia. This was postulated on the basis of the following observations:

1. The absence of the physiologic creatinuria of infancy and childhood in a patient with myotonia congenita.

Fig. 6.—Photograph of the patient (M. D.), aged 22 years, showing extreme hypertrophy of the muscles.

2. The relief of myotonia and muscle hypertrophy when the excretion of creatine was established at a normal level by the administration of thyroid.

3. The return of myotonia and muscle hypertrophy when the excretion of creatine was diminished.

4. The production of myotonia by ingestion of creatine when the patient was free from symptoms.

The question was raised as to how these observations can be applied to adult male patients, in whom creatinuria is normally absent, who suffer from myotonia congenita.

A man aged 22 with classic myotonia congenita (Thomsen's disease) was referred to us, by Dr. Soma Weiss, for study. On a creatine-free diet this patient excreted no creatine, and his creatinine excretion was just above the limits of the normal, as determined by various observers. When creatine was given by mouth in doses of 3 Gm. daily for five days there was complete retention of creatine and no increase in the excretion of creatinine. The retention of 15 Gm. of creatine is, of itself, not abnormal in an adult patient,[19] but the fact that none of the substance, either as creatine or as creatinine, appeared in the urine is significant. In the adult patient studied, as in the infant, the myotonia was accentuated during the period of ingestion of creatine. There was, however, a great difference in the responses of the two patients to thyroid or thyroxine. In the infant the administration of thyroid was followed by relief from the myotonia and the excretion of creatine in

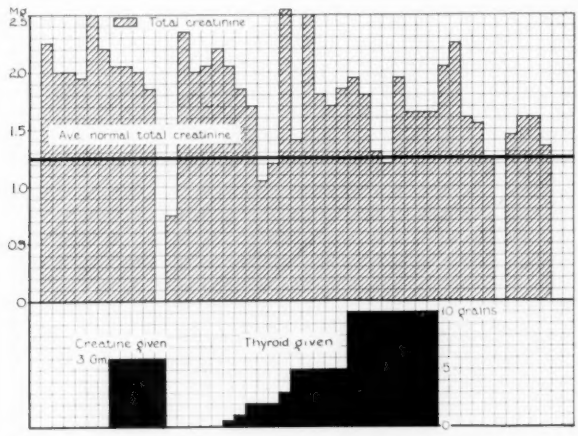

Fig. 7.—Chart showing the excretion of creatinine for the patient (M. D.) at 22 years of age. Note that the administration of creatine neither produced creatinuria nor increased the amount of creatinine excreted and that the giving of thyroid also failed to produce creatinuria.

the urine, whereas in the adult there was neither creatinuria nor relief of symptoms but rather an accentuation of the myotonia. This observation was constant when doses of thyroid up to 10 grains daily were given. The calorigenic response of the adult patient to thyroid was normal, however.

In the present state of information a conclusive explanation of the difference in therapeutic response cannot be offered, but there are numerous observations that may be considered correlatively. While myotonia congenita occurs in childhood and may be observed even in

19. Hunter, A.: Creatine and Creatinine, London, Longmans, Green & Co., 1928, p. 140.

early infancy, the symptoms usually become accentuated or appear first at puberty or in early adult life. This has been pointed out by many observers.[9] Although the time of disappearance of the physiologic creatinuria of childhood shows wide individual variations, the change is usually associated with puberty and has been ascribed to alteration in the endocrine system incident to that period.[20] We have observed a juvenile type of creatine metabolism in a woman in whom on postmortem examination entire absence of ovarian tissue was noted and have also seen an adult type of creatine metabolism in a 6 year old child with precocious sexual and osseous development. Observations of this nature have been made by other investigators [21] also. The question as to whether the difference in creatine metabolism between children and adults is sufficient to account for the variation in the therapeutic response to thyroid and thyroxin in the cases here described cannot be settled by the study of only two cases or by abstract reasoning from reports in the literature but requires further investigation.

Our first attack on the solution of this problem was the attempt to find out why treatment with thyroid or thyroxin is apparently successful in children with myotonia congenita. The fact was noted quite by accident. We had observed, as had others,[22] that creatine was absent or noticeably diminished in the urine of untreated hypothyroid children but appeared in approximately normal amounts when thyroid was given. In studying the infant with myotonia congenita it was noted that the administration of thyroid induced creatinuria and that, coincident with it, there was clinical improvement. Was the patient deficient in thyroid, or did the thyroid affect him in some unsuspected manner?

Close examination revealed no evidence on which to base an affirmative answer to the first part of this question. Epiphysial development, the texture of the hair and the skin, muscular development and tone, the blood cholesterol content and other factors were against a diagnosis of hypothyroidism. The delayed development, the large, thick tongue and the absence of creatinuria were the only manifestations compatible with such a diagnosis. Since the infant was given thyroid at an early age, the point may be raised that the classic signs of hypothyroidism perhaps were obscured by the replacement therapy. Opposed to this

20. Rose, W. C.: The Metabolism of Creatine and Creatinine, in Luck, J. M.: Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1935, vol. 4, p. 253.

21. Beumer, H., and Fasold, H.: Der Abbau alimentären Kreatins als spezifische Reaktion des geschlechhtsreifen Organismus, Klin. Wchnschr. **10**:937, 1931. Fasold, H.: Ueber den Kreatinstoffwechsel bei Pubertas praecox, Ztschr. f. Kinderh. **51**:527, 1931.

22. Beumer, H., and Iseke, C.: Der Kreatin-Kreatininstoffwechsel bie Myxödem und gesunden unter Einwirkung von Thyreoidin, Berl. klin. Wchnschr. **5**:178 (Feb.) 1920.

view is the fact that from the age of 1 year for nearly ten months the child was given no thyroid, and he learned to walk and talk normally. It is not likely that an infant with congenital hypothyroidism would develop in such a manner. While there are not many detailed reports of the cases of persons with myotonia congenita in infancy, the available reports point out the delay in sitting up and in learning to walk and talk and the presence of a large, thick tongue. Friis [23] reported the cases of a father and two children with myotonia congenita. In both children the disease was noted in early infancy. One had difficulty in nursing at the breast because of a large thick tongue. This child also was small and had a thick flat nose and short thick neck. The other infant erupted his first tooth when he was 9 months of age and showed much delay in learning to walk.

Recently, however, Debré and Sémelaigne [24] reported the cases of two infants showing diffuse muscular hypertrophy and hypertonia and discussed the connection of these symptoms with congenital myxedema. They did not refer to them as examples of myotonia congenita or Thomsen's disease but considered them as a syndrome of diffuse muscular hypertrophy and hypertonia due to congenital athyroidism. In one patient the wrinkled forehead, flat nose, swollen eyelids, thick lips and large tongue, the absence of hair on the eyebrows and the scalp, the arrested growth and the mental retardation, in spite of the thin skin, favored the diagnosis of congenital hyperthyroidism. Debré and Sémelaigne regarded the muscular hypertrophy as being due to "an overcharge of the muscles of a metabolic order and of neuroendocrine origin." One of the patients, a girl aged 2 years, was given the equivalent of about ⅓ grain (0.02 Gm.) of thyroid daily and when seen six months later she looked like a normal baby. The limbs had lost the muscular hypertrophy, and no hypertonia was present. It is difficult to classify the cases on the basis of the facts presented, but the demonstrated relationship between treatment with thyroid and the muscular hypertrophy and hypertonia is pertinent.

The question was raised by Debré and Sémelaigne as to whether this clinical syndrome is not based on congenital hypothyroidism, and they attempted to classify the cases reported by de Lange [25] and Bruck [26] in

23. Friis, A. : Zur Kenntnis der Thomenschen Krankheit (Myotonia congenita), Zentralbl. f. d. ges. Neurol. u. Psychiat. **11**:40, 1892.

24. Debré, R., and Sémelaigne, G.: Syndrome of Diffuse Muscular Hypertrophy in Infants Causing Athletic Appearance: Its Connection with Congenital Myxedema, Am. J. Dis. Child. **50**:1351 (Dec.) 1935.

25. de Lange, Cornelia: Congenital Hypertrophy of Muscles, Extrapyramidal Motor Disturbances and Mental Deficiency: Clinical Entity, Am. J. Dis. Child. **48**:243 (Aug.) 1934.

26. Bruck, F.: Ueber einen Fall von congenitaler Makroglossie combiniert mit allgemeiner wahrer Muskelhypertrophie, Deutsche med. Wchnschr. **15**:229, 1889.

this category. De Lange's report concerned three unrelated infants with congenital hypertrophy, extrapyramidal motor disturbances and mental deficiency seen in her clinic, and she also cited a comparable case reported by Bruck. In one of de Lange's cases autopsy showed definite lesions of the central nervous system. She said the cerebral lesions and muscular hypertrophy might be related but expressed a desire to study other cases before committing herself definitely to that view. There was some resemblance to Thomsen's disease, but the clinical picture as a whole was different.[27] The condition in the cases of de Lange and Bruck would appear to correspond to what Erb in his classification of myotonia designated as myotonia associated with involvement of the nervous system and not true Thomsen's disease. Myotonia and muscular hypertrophy may occur in other disorders besides Thomsen's disease, and the grouping of cases into one etiologic category solely on the basis of muscular hypertonia and hypertrophy may lead to confusion.

The question as to the relationship of hypothyroidism to muscular hypertrophy and hypertonia is difficult to settle at the present time. We have never observed muscular hypertrophy and hypertonia in a large group of untreated hypothyroid children; furthermore, administration of creatine to such children is without apparent influence on the muscles. We have not been able to observe myotonia in untreated hypothyroid children even when they received creatine in doses of 3 Gm. daily for as long as two weeks.

The fact that children with muscular hypertrophy and hypertonia respond to treatment with thyroid is no proof that the condition of all patients showing such symptoms is based on hypothyroidism. The first mention of the use of thyroid in the treatment of myotonia congenita was in Jensen's article published in 1903.[10] Since that time many comprehensive discussions of myotonia congenita have mentioned thyroid among the substances advised for use in the treatment of the disease [28] but the drug has not received much favorable comment as a therapeutic agent in treating adult patients. Our observation of one adult with Thomsen's disease confirms the attitude of earlier writers on this point. But while investigation of the case of the infant here reported was in progress, Valdés Díaz,[29] in Cuba, reported the case of a Negro male infant with myotonia congenita who was successfully treated with thyroid. The disorder was first manifested thirty days after the child's birth by extraordinary firmness of the abdominal muscles. At 3 months of age the infant had generalized muscular hypertrophy and presented a

27. Personal communication to the authors.

28. White, W. A., and Jelliffe, S. E.: Modern Treatment of Nervous and Mental Diseases, Philadelphia, Lea & Febiger, 1913, vol. 2, p. 137. Steiner.[7]

29. Valdés Díaz, R.: Miotonia congénita (enfermedad de Thomsen), Arch. de med. inf. **1**:15, 1932.

Herculean aspect. Valdés Díaz noted the high creatinine content of the patient's blood, but the creatine-creatinine excretion was not studied. When the patient was treated with thyroid the myotonic symptoms and muscular hypertrophy disappeared. We wrote to Valdés Díaz in an effort to have him study the creatine-creatinine metabolism of his patient, but the infant and his family had left Havana during the revolution and had disappeared into the interior. Valdés Díaz in photographs of his patient showed the muscular hypertrophy vividly, and his description was typical of a sporadic case of myotonia congenita. There was, however, no evidence of hypothyroidism in the clinical picture or in the child's appearance.

Finally, we were confronted with the fact that hypothyroidism was not associated with Thomsen's disease in any of the hundreds of cases reported. Whether the cases described by Debré and Sémelaigne are an exception to this statement would depend on whether they can be regarded as examples of myotonia congenita. There was no discussion of differential diagnosis in their report.

In a personal communication from Nevin concerning his investigation of the chemistry of the muscles [30] in various myopathies he told of the study made of a girl, aged 17, with a possible diagnosis of myotonia congenita. Clinically, enlargement of the muscles and myotonia were present. Chemical examination of the muscle removed at biopsy showed some changes in the phosphorus-holding compounds, in that the creatine phosphoric acid during rest was somewhat below normal, and the changes on contraction were less than normal. In the meantime, because there was a history of cretinism, thyroid was administered to the patient, who had not taken any for some time, and this resulted in such improvement in the muscle that it was no longer possible to consider the case one of myotonia congenita. Studies of action currents in the muscle also led Nevin to believe that the disorder was different from Thomsen's disease. He called our attention to the report of a case by Weitz,[31] who described muscular symptoms in an adult with myxedema. The patient was a physician, 44 years old, who had received treatment with roentgen rays over the thyroid gland for hyperthyroidism. Subsequently, a subtotal thyroidectomy was performed, and the myxedema associated with hypertonia and muscular hypertrophy developed postoperatively. Clinical and laboratory examinations revealed no evidence of tetany, and the symptoms quickly abated on treatment with

30. Nevin, S.: Study of Muscle Chemistry in Myasthenia Gravis, Pseudohypertrophic Muscular Dystrophy and Myotonia, Brain **57**:239, 1934.

31. Weitz, W.: Ueber eigentümliche Muskelerscheinungen bei Myxödem (das nach Röntgenbestrahlung und teilweiser Strumektomie entstanden war), Deutsche Ztschr. f. Nervenh. **120**:297, 1931.

thyroid. While there was definite myotonia on mechanical percussion, the disease differed from myotonia congenita in that pain accompanied the myotonia, and electrical excitability of the nerves, as well as of the muscles, was present.

From these facts it would appear that there are cases of hypothyroidism with myotonia but that such cases must not be confused with those of true myotonia congenita. The success of treatment with thyroid in children with myotonia congenita and in patients of all ages with myotonia associated with hypothyroidism may, however, be due to the same fundamental mechanism. There is abundant evidence of a relation between thyroid and the metabolism of creatine, but a definite participation of the thyroid gland in the physiology of musclar contraction has not been established. However, a cycle of interrelated chemical changes accompanying muscular contraction and relaxation has been demonstrated. A breaking down of creatine phosphate is associated with the beginning of muscular contraction, and this compound is resynthesized during the phase of recovery. The latter process is energized by the transformation of glycogen to lactic acid, and this change involves a series of intermediate compounds, the nature of which depends on whether oxygen is present or not. An abnormality of any part of this cycle might account for the abnormal metabolism of creatine in myotonia. This metabolism may involve the action of thyroid directly or indirectly.

In the presence of normal function of the thyroid gland the administration of thyroid has been shown to have the following effects which might influence muscular metabolism:

1. Experimentally, the feeding of preparations of thyroid to rats has resulted in a reduction of creatine in the muscles.[32]

2. The giving of thyroid or thyroxin increases the basal metabolic rate, which in the absence of the adequate ingestion of protein and carbohydrates results in a negative nitrogen balance and glycolysis.

3. A decrease in the glycogen in the muscles with the use of thyroxin was demonstrated recently by Brentano.[33] He found that creatinuria is associated with a decrease in the glycogen in the muscles, and that there is an increase in the glycogen when experimentally induced creatinuria ceases. It may be that, with the greater ease with

32. Abelin, I., and Spichtin, W.: Ueber den Einfluss der Schild-drüsensubtanzen auf den Gesamtkreatiningehalt der Leber und des Muskels, Biochem. Ztschr. **228**:250, 1930. Bodansky, M.: Effect of Thyroid and Thyroxine on the Concentration of Creatine in the Heart, Muscle, Liver, and Testes of the Albino Rat, J. Biol. Chem. **109**:615 (May) 1935.

33. Brentano, C.: Zur klinischen Bedeutung der Kreatinurie, Deutsche med. Wchnschr. **58**:699, 1932.

which glycogen is utilized in a patient under treatment with thyroid, muscular relaxation [34] and recovery are more prompt.

4. The administration of thyroxin increases the consumption of oxygen in the tissues, including the muscles. Recent observations have shown that the increase in the consumption of oxygen in the intact animal produced by thyroxin is due to its effect on the tissues themselves and that this effect persists when the tissues are isolated from the animal.[35]

Further data are necessary, however, before these observations can be applied directly to the treatment of patients. Moreover, the information does not explain adequately why adults with myotonia congenita do not respond as do infants to treatment with thyroid or thyroxin, or why hypertonia and muscular hypertrophy are not encountered more commonly in patients with hypothyroidism.

SUMMARY

A prolonged study of the creatine-creatinine metabolism of an infant with myotonia congenita (Thomsen's disease) revealed the following features:

1. The physiologic creatinuria of infancy and childhood was absent, although the patient was ingesting an adequate amount of protein.

2. Creatinuria appeared on the administration of thyroid, and the amount of creatine excreted appeared to have a relation to the size of the dose of thyroid.

3. The excretion of creatinine was not significantly affected by the administration of thyroid.

4. A carefully controlled dosage of thyroid rendered the patient symptom-free.

5. The administration of 1 Gm. of creatine by mouth while the patient was symptom-free caused a return of the myotonia, although an approximately normal proportion of the ingested creatine was excreted.

6. A decrease in the amount of creatine excreted was invariably associated with myotonia. Either condition might appear first.

7. In spite of the fact that the patient was receiving thyroid, infections (whooping cough and measles) caused a decrease in the amount of creatine excreted and a return of the myotonia.

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34. Grégoire, P.-E.: De l'influence de la thyroxine sur la glycolyse du tissu musculaire, Compt. rend. Soc. de biol. **122**:103, 1936.

35. McEachern, D.: Metabolism of Isolated Surviving Tissues from Animals Rendered Hyperthyroid with Thyroxine, Bull. Johns Hopkins Hosp. **56**:145 (March) 1935.

8. An increase in the dose of thyroid relieved the myotonic symptoms even in the presence of infection.

9. The amount of creatine excretion remained small during the persistence of the infectious conditions, in spite of an elevation of temperature.

NOTE.—Since this article was submitted for publication, Hall, Sunderman and Gittings [36] have reported a case of the syndrome of congenital muscular hypertrophy, extrapyramidal motor disturbances and mental deficiency in a 3 year old Negro boy. Their report is a confirmation of the point made in this paper that myotonia or muscular hypertrophy may occur in other disorders besides Thomsen's disease and that the grouping of cases into one etiologic category solely on the basis of muscular hypertonia or hypertrophy may lead to confusion.

The author's findings of an abnormally high excretion of creatine and creatinine in the urine, complete excretion of 0.5 Gm. of ingested creatine within forty-eight hours and high values for potassium, inorganic phosphorus and phosphatase in the serum are in marked contrast with the findings reported in our case and give additional aid in the differential diagnosis of congenital hypertrophy or myotonia in infants.

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36. Hall, B. E.; Sunderman, F. W., and Gittings, J. C.: Congenital Muscular Hypertrophy, Am. J. Dis. Child. **52**:773 (Oct.) 1936.

VENOUS PRESSURE IN CHILDREN

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The present study was made to determine the normal range of venous pressure in children. The diagnostic and prognostic value of determinations of venous pressure in adults is well established. It has been shown that beginning myocardial incompetency is reflected by an increase in the venous tension. Through studies of venous pressure [1] much has been learned concerning cardiac function, edema and the exchange of material through the capillary walls. Criep [2] and Hooker [3] have noted a variation in venous pressure with age, though only a few observations in the younger age group are reported. In a review of the literature I was unable to find any series dealing solely with children. For these reasons, readings of venous pressure were made on certain of the children admitted to the Babies Hospital.

The observations were limited to children between the ages of 4 and 13 years. The group was composed mainly of surgical and otolaryngologic patients. A large proportion were admitted solely for tonsillectomy and so approximate a random sampling. All patients were carefully studied by clinical and laboratory methods, with special attention to the cardiovascular and pulmonary status. No patient was included in the series in whom there was any indication of myocardial damage or pulmonary disease.

The direct method apparatus (of Moritz and von Tabora [4]) was used, the needle being inserted proximally into the antecubital vein. The patient was always in the recumbent position with the arm level at the side. The zero point on the manometer scale was leveled with the second intercostal space to the right of the sternum. The distance from this point to the right auricle as determined by measurement of necropsy material ranges between 15 and 20 mm. In this series 17 mm. was taken as a standard and was included in each reading. The needles used varied from 18 to 20 gage. Readings were repeated until they agreed within 2 mm.

From the Babies Hospital.

1. Krogh, A.; Landis, E. M., and Turner, A. H.: Movement of Fluid Through Human Capillary Wall in Relation to Venous Pressure and to Colloid Osmotic Pressure of Blood, J. Clin. Investigation **11**:63, 1932; Celluloid Capsule for Measuring Venous Pressure, ibid. **11**:357, 1932.

2. Criep, L. H.: Studies of Venous Pressure: Their Clinical Application, M. Bull. Vet. Admin. **8**:463, 1932.

3. Hooker, D. R.: Observations on the Venous Blood Pressure in Man, Am. J. Physiol. **35**:73, 1914; The Influence of Age upon the Venous Blood Pressure in Man, ibid. **40**:43, 1916.

4. Moritz, F., and von Tabora, D.: Ueber eine Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, Deutsches Arch. f. klin. Med. **98**:475, 1910.

Preliminary studies were made to permit evaluation of the effect of two possibly disturbing factors: (1) the size of the needle and (2) the degree of cooperation on the part of the patient. Table 1 shows the results obtained with various needles. Although the use of a smaller needle increased the tendency to clot, all sizes of needles employed were satisfactory. However, it was noted that the fluid in the manometer reached the basal level more slowly with the smaller needles.

In many instances the child cried and struggled during venipuncture. Such exercise undoubtedly increases the venous return to the heart; however, it has been shown [5] that provided there is no myocardial damage such an increase in the extrinsic load is immediately handled by an increased cardiac activity so that only a momentary rise, if any at all, occurs. This, of course, does not hold true for strenuous and prolonged exertion. It was also appreciated that with crying

TABLE 1.—*Venous Pressure with Various Needles*

Subject	Needle Gage	Venous Pressure, Mm. Water
P. C.	18	43
	19	42
	20	43
	21	43
	22	Clotted
G. S.	18	37
	19	38
	20	36
	21	37
	22	37
F. K.	18	51
	19	50
	20	51
	21	50
	22	Clotted

TABLE 2.—*Comparison of Venous Pressure With and Without Anesthesia*

Subject	Venous Pressure, Mm. Water	
	With Anesthesia	Without Anesthesia
E. G.	56	57
J. K.	43	42
L. W.	60	60

alteration in the intrathoracic pressure occurs, the increased inspiratory effort tending in general to lower venous pressure and the expiratory phase to raise it. In a few instances there was some fluctuation of the fluid level in the manometer reflecting such alterations in the intrathoracic pressure, but in the main the range was insignificant. The possible effect of overventilation with resultant hypercapnia leading to increased venous pressure has not been considered important. The children were given sufficient time to become accustomed to the presence of the needle, and they usually were at ease before final readings were obtained. It was possible to repeat readings during anesthesia on three children who had been resistant. These data are shown in table 2. It was concluded that small needles and poor cooperation did not significantly influence the final readings.

5. (*a*) Henderson, Y., and Barringer, T. B.: The Relation of Venous Pressure to Cardiac Efficiency, Am. J. Physiol. **31**:352, 1913. (*b*) Caughey, J. L., Jr.: Effect of Rapid Infusion on Venous Pressure: Test of Cardiac Reserve, Proc. Soc. Exper. Biol. & Med. **32**:973, 1935.

The results of the determinations of venous pressure in one hundred children are presented in chart 1 in a frequency diagram. The mean value is 48.4 mm. of water, and the median value is 47.2 mm. of water. The standard deviation from the mean is ± 9.5 mm. of water.

In table 3 are listed a few of the values for normal adults as reported in the literature. The discrepancy in the normal ranges would undoubtedly be much less if the same method had been used by all the observers. The influence of hydrostatic pressure is of considerable importance; part of the variation is caused by the difference in methods used to control this factor. Because of the variations which depend on method and because no report familiar to me has expressed the normal range in the form of a mean value and standard deviation, it is impossible to make a close comparison between the findings in this series of children and those previously reported for adults. The measurements of Moritz and von Tabora,[4] Caughey [5b] and Griffith and his collaborators [6] were

TABLE 3.—*Normal Range of Venous Pressure in Adults*

Observer	Method	Range, Mm. Water
Owens: J. Lab. & Clin. Med. **18**: 266, 1932	Indirect	35-90
Eyster and Middleton: Arch. Int. Med. **34**: 228 (Aug.) 1924	Indirect	50-60
Runge: Arch. f. Gynäk. **22**: 142, 1924	Indirect	48-66
Moritz and von Tabora [4]	Direct	40-80
Berghausen: J. Med. **15**: 22, 1934	Direct	40-80
Caughey [5b]	Direct	40-80

made by the same technic as that used by me with the exception that a larger correction was used for the distance from the heart to the anterior wall of the chest. With allowance for this fact the data do not warrant the conclusion that a significant difference exists between the venous pressure of normal children between the ages of 4 and 13 years and that of normal adults.

In chart 2 the individual pressure readings for this series are plotted according to age. The graph shows no obvious simple relationship between venous pressure and age.

This study has been concerned chiefly with children showing normal circulatory performance. A few determinations in patients with disease of the myocardium have indicated the manner in which the circulatory

6. Griffith, G. C.; Chamberlain, C. T., and Kitchell, J. R.: Simplified Apparatus for Direct Venous Pressure Determination Modified from Moritz and v. Tabora, Am. J. M. Sc. **187**:371, 1934; Observation on Practical Significance of Venous Pressure in Health and Disease with Review of Literature, ibid. **187**: 642, 1934.

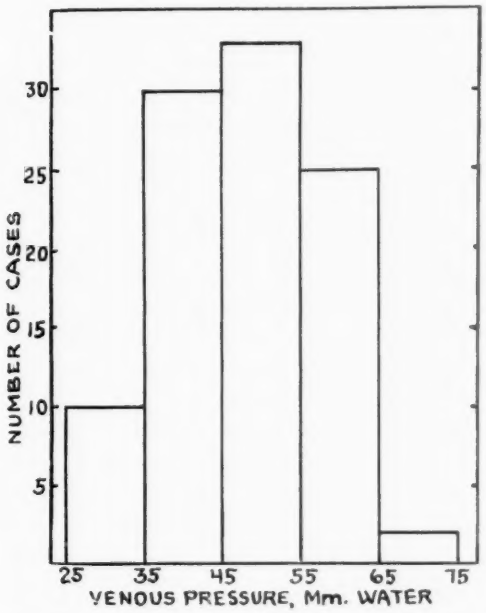

Chart 1.—Distribution of venous pressures according to frequency in one hundred children.

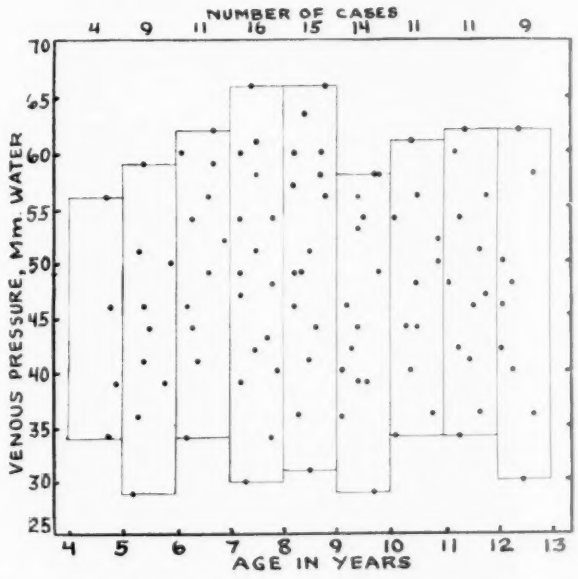

Chart 2.—Comparison of venous pressures according to age.

insufficiency is reflected in the pressure in the veins. A sample case illustrating this point is the following:

An 8½ year old white girl (B. H.) was admitted because of chorea. Physical examination revealed classic signs of stenosis and insufficiency of the mitral valve; the lungs were normal, but the liver was slightly enlarged; no edema of the extremities was noted. The venous pressure was 130 mm. of water.

SUMMARY

Determinations of venous pressure were made on one hundred normal children between the ages of 4 and 13 years by the direct method apparatus of Moritz and von Tabora. It was shown that variations (within certain limits) in needle bore and in the degree of cooperation of the patient do not affect significantly the values recorded. The average venous pressure was 48.4 mm. of water; the range is indicated by a standard deviation of ± 9.5 mm. of water. No relationship between age and venous pressure was found.

THE RATE OF SEDIMENTATION OF THE ERYTHROCYTES IN RHEUMATIC INFECTION IN CHILDREN

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Observations regarding the rate of sedimentation of the erythrocytes are sufficiently ancient to lend dignity and interest to the problem offered by the variation of this rate in rheumatic infection in children. Galen [1] recorded that in certain conditions, particularly in severe infections, blood rapidly settled out, leaving a clear yellow serum. Several other clinicians made similar comments during the period when "blood letting" was popular. These observations were not crystallized into a test of value until 1897, when Bienacki [2] proposed a method of measuring the speed with which red cells were separated from the plasma. There have been numerous modifications of his method, and the names of Fahraeus, Westergren and Linzenmeier are familiar in the literature on the subject. The basis of all the tests suggested is the time required for the erythrocytes to settle out of their suspension in the plasma. Fahraeus explained the change in the rate of sedimentation as due to variation in a property of the plasma, i. e., to a qualitative change in serum globulin, principally fibrinogen. On the other hand, Ernstene [3] showed that the important factor influencing the rate was the quantitative variation in the fibrinogen. The amount of fibrinogen and the rate of sedimentation of the erythrocytes are increased in many diseases, such as suppurative processes, contagious diseases, rheumatic infection, pneumonia, tuberculosis, syphilis, anemia [4] and leukemia. The fibrinogen is decreased in degenerative lesions of the liver. Venous stasis is another important cause of decrease in the rate of settling out of the red cells.

From the Cardiac Service of Dr. Stanley Gibson, the Children's Memorial Hospital.

1. Galen, cited by Waugh, T. R.: The Blood Sedimentation Test: Its History, Technique, Nature and Clinical Application, Canad. M. A. J. **13**:604-608, 1923.

2. Bienacki, cited by Peterman, M. G., and Seeger, S. J.: Sedimentation Reaction in Children, Am. J. Dis. Child. **37**:693-719 (April) 1929.

3. Ernstene, cited by Gilligan, D. R., and Ernstene, A. C.: Relationship Between Sedimentation Rate and Fibrinogen Content of Plasma, Am. J. M. Sc. **187**:552-556 (April) 1934.

4. Hubbard, H. S., and Geiger, H. B.: Anemia as a Factor in the Sedimentation Time of Erythrocytes, J. Lab. & Clin. Med. **13**:322-326 (Jan.) 1932.

Distinct variations in the rate of sedimentation on account of such physiologic processes as digestion and thirst have been reported. External heat and medication also modify the rate. The quantity of fibrinogen and the sedimentation rate are increased in the female during the premenstrual and menstrual phases of the cycle.

Many investigators have utilized tests to determine the rate of sedimentation of the erythrocytes in the practice of pediatrics. However, reports on the application of such a test in cases of rheumatic infection [5] are relatively few and are based on a limited number of cases. The results obtained indicate that the test is of prognostic as well as of diagnostic value.

The present study was undertaken in May 1934, at the suggestion of Dr. Stanley Gibson, director of the cardiac service at the Children's Memorial Hospital. An attempt was made to correlate the clinical course with the rate of sedimentation of the erythrocytes in children having rheumatic infection. The stimulus for this work was the need for a reliable means of determining the presence and degree of rheumatic infection. If the rate proved dependable for this purpose, it would be of service in determining the beginning of convalescence.

It was decided that a test of the rate of sedimentation should be made at the time of the patient's admission to the hospital and as frequently thereafter as necessary in order to follow the clinical progress, rather than at regular intervals regardless of the clinical course. For example, a patient who showed a rapid sedimentation rate, fever, a rapid pulse, arthritis and nodules when he was admitted to the hospital would not be tested again until his symptoms showed some signs of improvement.

At the same time the test of the rate of sedimentation was made a complete blood count, including a Schilling differential count, was made. The general condition of the patient was noted as to color, appetite, temperature, pulse, swollen or tender joints, annular erythema and cardiac damage.

The technic used was Banyai's [6] modification of the Westergren method. Into a 2 cc. syringe is drawn 0.4 cc. of 3.8 per cent solution of sterile sodium citrate. A

5. Ernstene, A. C.: Erythrocyte Sedimentation, Plasma Fibrinogen and Leukocytosis as Indices of Rheumatic Infection, Am. J. M. Sc. **180**:12-24 (July) 1930. Elghammer, H. W.: Erythrocyte Sedimentation Rate in Rheumatic Infections, Arch. Pediat. **51**:250, 1934. Rogatz, J. L.: Comparative Value of the Schilling Differential Blood Count and the Sedimentation of Erythrocytes in Acute Rheumatic Fever in Childhood, J. Pediat. **8**:184-192 (Feb.) 1936. Payne, W. W., and Schlesinger, B.: A Study of the Sedimentation Rate in Juvenile Rheumatism, Arch. Dis. Childhood **10**:403-414 (Dec.) 1935.

6. Banyai, A. L., and Anderson, S. V.: Erythrocyte Sedimentation Test in Tuberculosis: Study of Two Thousand Cases, Arch. Int. Med. **46**:787-796 (Nov.) 1930.

venipuncture is done without constricting the arm, and the syringe is accurately filled with blood, care being taken to keep the blood from going beyond the graduated portion. A bubble of air is then drawn into the syringe, and it is inverted several times, until the blood and citrate are well mixed. The liquid is then transferred to a 1 cc. glass tube, graduated so that 100 is at the top, and the height of the column of erythrocytes can be easily read. These determinations are made at the end of fifteen minutes, thirty minutes, one hour and two hours. The following figures represent the average readings for normal persons: 97, 95, 90 and 75. Their sum, plus the constant 43, divided by 4, gives 100 per cent, or normal. Also a graph may be plotted with the time as the abscissa and the height of the column of erythrocytes as the ordinate. The method proved satisfactory, and the results quoted will be expressed as percentages of the normal.

The venipuncture has been the chief cause for criticism of this method. As astonishing as it may seem, the children in the ward ask for a test not only because they welcome any attention which relieves the monotony of the day but because they have learned that the making of a test is an indication of progress which may lead to increased liberty or even to going home. Only the very ill patient who is suffering from acute pericarditis or congestive heart failure objects. He also protests when his temperature is taken or he is given other necessary care.

This study includes the observations of 140 patients—the majority of those admitted to the cardiac service from May 1934 to November 1935. Five hundred tests were made, 338 of them during the period of clinical activity of the rheumatic infection.

In an attempt to correlate clinical with laboratory findings it became apparent that certain divisions had to be made. The cases were grouped, according to diagnosis, as follows:

1. Chorea not associated with arthritis or carditis.
2. Active rheumatic infection without signs of carditis.
3. Active rheumatic infection preceded or followed by chorea.
4. Active rheumatic infection with carditis.
5. Active rheumatic infection with congestive heart failure.

OBSERVATIONS

Chorea Not Associated with Arthritis or Carditis.—Chorea as the sole manifestation of the rheumatic process was found to be characterized by a normal rate of sedimentation of the erythrocytes. There were 19 cases of this condition. The average sedimentation rate during the period of activity was 94 per cent. Five of the patients had severe incoordination, so that the taking of food was difficult. In these severe cases phenylethylhydantoin was prescribed. The dose was 5 grains (0.3 Gm.) daily for fourteen days, or until fever developed. This medication produced a gradual sedation so that by the fourth day the patient struggled less, ate better and slept more. When the full thera-

peutic effect was obtained, as evidenced by fever and a morbilliform eruption, a characteristic blood picture [7] was seen: a rapid sedimentation rate, proportional to the clinical reaction, leukopenia and eosinophilia.

The average sedimentation rate during the febrile reaction was 82 per cent. The rate was higher when the temperature reached a high point. It is interesting that the rate was rapid when a rash appeared, even in the absence of fever.

The leukocyte count prior to medication was normal in practically every case. The count was depressed in proportion to the severity of the systemic reaction to the drug. In one case the temperature rose to 104 F. and the leukocyte count was 3,000.

Eosinophilia has been observed as characteristic of the blood picture during the therapeutic effect of phenylethylhydantoin. We found a variation from 5 to 15 per cent.

Active Rheumatic Infection Without Signs of Carditis.—Clinically, the patients with acute rheumatic manifestations had a temperature from 101 to 103 F. and acute polyarthritis in which the pain, swelling and tenderness involved successive joints, particularly the large ones. At no time were there evidences of acute carditis. Of the 10 cases studied, the average duration of the infection as measured by the sedimentation rate was two months. The following case is summarized as an example:

A girl 6 years old was admitted to the hospital May 28, 1934, with a history of polyarthritis for one week. The polyarthritis had been preceded by nasopharyngitis. The elbows, knees, wrists and ankles had been successively involved, presenting swelling, tenderness and limitation of motion. The patient had an elevation of temperature to 103 F., a pulse rate of 120 per minute and no auscultatory evidence of carditis. The blood count showed hemoglobin (Sahli) 53 per cent, erythrocytes 3,800,000 and leukocytes 29,000. The differential count was as follows: polymorphonuclears 75 per cent, with 20 stab forms, lymphocytes 20 per cent, mononuclears 4 per cent and eosinophils 1 per cent. The rate of sedimentation of the erythrocytes was 53 per cent. After one week of rest in bed and treatment with acetylsalicylic acid the pains and swelling in the joints subsided. The temperature, as would be expected, returned to normal. The leukocyte count dropped to 20,000, and the sedimentation rate became less rapid (64 per cent). The Schilling differential count reflected the improvement also, with a decrease to 16 per cent of stab forms. The medication was discontinued. Two weeks later the temperature and the pulse were normal. The sedimentation rate was 87 per cent, the leukocyte count had decreased to 10,000 and the Schilling differential count was normal. Although the patient appeared convalescent, the sedimentation rate indicated the presence of slight infection. However, one week later (five weeks after the onset of arthritis) the sedimentation rate was normal.

In the average case monocyclic rheumatic infection can be expected to subside within two months of the onset. This is in accord with the

7. Monfort, J. A.: Chorea Treated with Phenyl-Ethyl-Hydantoin and Typhoid Vaccine: A Comparative Study, Am. J. Dis. Child. **47**:1269-1278 (June) 1934.

results of Ernstene's [5] study. The rate of sedimentation of the erythrocytes is rapid during the period of clinical activity, averaging 77 per cent, and also for two weeks or more after all clinical evidences of infection have subsided. The number of leukocytes and the Schilling differential count parallel the clinical course of the infection, in most instances becoming normal before the erythrocytes show a normal rate of sedimentation. For a long time one of the major problems in the care of the patient with rheumatic infection has been the determination of the beginning of convalescence. Not knowing just when the infection subsided, the physician has had no choice but to follow the only safe procedure he knew and prescribe a prolonged period of rest in bed. Now, if one may rely on the rate of sedimentation of the erythrocytes to reflect the presence of rheumatic infection, it can be determined when infection has subsided, and the activity of the patient may be gaged accordingly.

Active Rheumatic Infection Preceded or Followed by Chorea.—It has often been emphasized that chorea and other symptoms of "rheumatism" do not occur simultaneously, but that the arthritis or carditis precedes or follows the active manifestations of chorea.

There were 14 patients in the series in whom chorea developed after a definite period of arthritis or carditis. The average sedimentation rate during the height of the chorea was 83 per cent. There were 4 patients who had a normal rate during the early period of chorea but later showed a more rapid rate. In their cases the rate of sedimentation indicated activity of infection two weeks before the appearance of symptoms or signs of carditis. One child had a sudden drop in the rate from 91 to 54 per cent. Four days later a pericardial friction rub could be heard.

Active Rheumatic Infection with Carditis.—Patients who had active rheumatic infection with carditis comprised the largest group—79 patients, for whom 201 sedimentation tests were made. The average rate during the period of clinical activity was 75 per cent. There were only 4 instances in which the rate was rapid during convalescence, as measured by the clinical appearance of the patient. The children were kept in bed until the rate was normal.

The 79 patients in this group presented blood pictures which varied widely. The leukocyte count varied from 6,000 to 28,000 during the height of the disease. The average was 12,000, with a preponderance of polymorphonuclear neutrophils and a moderate increase in stab forms (10 to 15 per cent).

The most rapid rates of sedimentation and the most marked increase in stab forms were found during acute pericarditis. The increase in the rate of sedimentation was sufficient to overcome the influence of venous stasis.

Nodules were present in 10 patients and were invariably an evidence of severe rheumatic infection. All of the children included in this study who had nodules also had prolonged infection of a severe type. The erythrocytes settled very rapidly in the tests made for these patients, the average rate being 77 per cent.

The annular erythema described by Lehndorff and Leiner [8] was present repeatedly in 6 children of the group having carditis and in 1 child who had nodules. The rate of sedimentation of the erythrocytes was invariably rapid. Two other patients were subject to erythema multiforme which was urticarial at times. Occasionally there was a normal sedimentation rate at the time of the eruption in this urticarial type of erythema multiforme, but a normal rate was never observed with the erythema annulare.

Before any of the patients having rheumatic infection were recommended for tonsillectomy, they were clinically convalescent and had normal rates of sedimentation of the erythrocytes. Determinations made on the first, second, third and fourth postoperative days showed that the sedimentation rate had remained normal, with an average of 98 per cent. There were no recurrences of infection which could be attributed to the surgical procedure.

Active Rheumatic Infection with Congestive Heart Failure.—The rate of sedimentation of the erythrocytes may or may not be rapid in patients with rheumatic infection and congestive heart failure. If the rheumatic infection was found to be extremely active, the rate remained rapid until cyanosis and venous stasis were considerable. All the normal rates occurring in these patients, of whom there were 14, were associated with marked edema and cyanosis.

Four of the patients were seen only after there were signs of a severe degree of congestive heart failure. Edema and cyanosis were sufficient to overshadow signs of active rheumatic infection. The sedimentation rate was normal or above normal. If these patients had been seen earlier, the evidences of active infection might have been apparent. The supposition that active rheumatic infection was present at the time of congestive heart failure was established by postmortem studies.

CONCLUSIONS

The rate of sedimentation of the erythrocytes was studied in an effort to determine the value of a test of the rate of sedimentation as a diagnostic and prognostic measure in cases of active rheumatic infection. The following conclusions seem justified:

8. Lehndorff, H., and Leiner, C.: Eruption with Endocarditis, Ztschr. f. Kinderh. **32**:46-53 (March) 1922. Lehndorff, H.: Das Erythema annulare rheumaticum, Wien. med. Wchnschr. **80**:1449 (Nov. 1) 1930.

Chorea is the only rheumatic manifestation characterized by a normal sedimentation rate.

Active rheumatic infection is characterized by a rapid sedimentation rate. This is true when arthritis or carditis occurs either alone or as a complication of chorea.

Acute pericarditis as a part of rheumatic carditis is accompanied by a very rapid sedimentation rate. This is true in spite of venous congestion.

The sedimentation rate is rapid in the presence of rheumatic nodules also. Judged by this, nodules are an expression of severe infection.

Annular erythema is found only during activity of the rheumatic infection and is associated with a rapid sedimentation rate.

Active rheumatic infection with congestive heart failure may be associated with a normal sedimentation rate when there is a high degree of venous stasis. Postmortem studies offered convincing proof of activity of the rheumatic infection in those cases in which the condition proved fatal.

The monocyclic rheumatic infection subsides in about two months, as measured by the rate of sedimentation of the erythrocytes. This is two weeks or more after the clinical manifestations have disappeared.

The Schilling differential count parallels the clinical course rather than the subsiding infectious process.

The sedimentation test is more reliable than the Schilling differential count in the diagnosis of the activity of the rheumatic process.

The sedimentation test may be used to determine the beginning of convalescence, as the clinical evidence of rheumatic infection disappears before the test indicates that the infectious process has subsided.

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RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

XIX. THE RESPIRATORY EXCHANGE IN PREMATURE INFANTS—ELIMINATION OF WATER THROUGH THE SKIN AND THE RESPIRATORY PASSAGES

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AND
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Data have been presented in previous papers of this series demonstrating that under standard conditions of indirect calorimetry infants and children lose an average of 26 and 24 per cent, respectively, of their basal heat production by vaporization of water through the skin and lungs.[1] The tendency to hypothermia exhibited by premature infants in the presence of a comparatively normal mechanism of heat production [2] suggested that they may dissipate an excessive fraction of their heat by vaporization.

To our knowledge the literature contains observations on only two premature infants, the average figure for four observations, each of from four to five days' duration, being approximately 46 per cent.[3] In our investigation the elimination of water from the skin and respiratory passages and the heat production of ten premature infants were determined.

APPARATUS AND METHODS

Simultaneous measurements of heat production and water elimination were made in fifty-one calorimetric observations of from three-fourths to two and one-half hours under standard conditions of clothing, diet, humidity and temperature. A description of the new respiratory chamber, the accessory apparatus and the methods for control of environmental temperature and humidity appeared in the previous paper of this series.[2] The experimental procedure, detailed calori-

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Levine, S. Z., and Wilson, J. R.: (*a*) Respiratory Metabolism in Infancy and in Childhood: IV. Elimination of Water Through the Skin and Respiratory Passages of Children, Am. J. Dis. Child. **33**:204 (Feb.) 1927; (*b*) VII. Elimination of Water Through the Skin and Respiratory Passages of Infants, ibid. **35**: 54 (Jan.) 1928.

2. Gordon, H. H., and Levine, S. Z.: Respiratory Metabolism in Infancy and in Childhood: XVIII. The Respiratory Exchange in Premature Infants—Basal Metabolism, Am. J. Dis. Child. **52**:810 (Oct.) 1936.

3. Rubner, M., and Langstein, L.: Energie u. Stoffwechsel zweier frühgeborener Säuglinge, Arch. f. Physiol. **39**:39, 1915.

metric data and the clinical criteria of prematurity for all except one infant [4] were presented in the same paper.

The average relative humidity of the respiratory chamber (determined by a hair hygrometer calibrated daily against a sling psychrometer) varied from 32 to 58 per cent (P45 and P2, table 1), the fluctuation during single periods of individual observations being from 1 to 6 per cent except in two observations, in which it was 10 per cent (P6 and P10). The change in average temperature in single periods of individual observations was between 0.03 and 0.48 C., the average temperature in individual observations ranging from 25.7 to 28.9 C. The average rectal temperature of the infants was between 36.2 and 37.3 C. (97.16 and 99.14 F.), the temperature changing less than 0.5 C. (0.9 F.) in all except five observations. In these (P2, P7, P8, P19 and P31) the change from the beginning to the end of the observation was from 0.6 to 1 C. (1.08 to 1.8 F.).

CALCULATION OF RESULTS

The heat production was calculated in the customary manner [5] from the oxygen consumption, the nitrogen excretion in the urine and the nonprotein respiratory quotient; in four instances, in which the oxygen determination was unsatisfactory, the carbon dioxide was used. The water elimination was directly measured, and the constant, 0.586 calories per gram of water, was employed to calculate the heat of vaporization. The relation between elimination of water through the skin and respiratory passages and heat production was expressed in terms of percentage of total calories vaporized.

ALCOHOL CHECKS

Observations were controlled by frequent alcohol checks, the details of which have already been published.[2] At an average rate of heat dissipation (6.91 calories per hour) comparable to that of the infants, the amount of water produced by the alcohol flame was only 1.3 Gm. per hour. The speed of ventilation required to stabilize the temperature in the respiratory chamber during the alcohol checks consistently led to a notable reduction in the relative humidity of the chamber. At the resulting low levels, frequently of only 10 per cent, water was extracted from the walls of the chamber, causing positive errors in the water determinations, which averaged + 9.3 per cent and ranged between + 4.4 and + 19.5 per cent for individual checks. The magnitude of the error could be appreciably reduced by preliminary drying and rapid closure of the chamber prior to the observation and by lowering the relative humidity of the air-conditioned room. For example, the error was only + 5 and + 6 per cent when the relative humidity of the room was 35 per cent (2/20/35 and 4/16/35) and + 16 when the humidity was 56 per cent (5/17/35).[2] Since the average amount of water necessary to produce a 10 per cent error in the alcohol checks was only 0.13 Gm. per hour, the source of error could well have been extraction of water from the walls of the chamber. Since, however, the average water elimination of the infants was more than twice that of the alcohol lamp, the speed of ventilation required to stabilize the temperature in the respiratory chamber during observations on infants permitted higher levels of relative humidity than those obtained in the alcohol checks. In the observations on infants the humidity averaged 42 per

4. H. B. (table 1) weighed 1,116 Gm. and was 39 cm. long at birth.

5. Zuntz, N., and Schumberg, W. A. E. F.: Studien zu einer Physiologie des Marsches, Berlin, A. Hirschwald, 1901, p. 361. Lusk, G.: Analysis of the Oxidation of Mixtures of Carbohydrate and Fat, J. Biol. Chem. **59**:411, 1924.

TABLE 1.—*Vaporization of Water in Premature Infants*

Subject	Date	Observation	Duration of Observation, Minutes	Number of Periods	Age, Days	Weight, Gm.	Calories per Hour	Water, Gm. per Hour	Percentage of Total Calories Vaporized		Average Temperature of Chamber, Centigrade	Average Relative Humidity of Chamber, Percentage
									In Individual Observation	Average		
P. C.	6/ 8/34	P 1	60	1	64	2,870	7.50	2.884	22.5		26.05	43
	6/14/34	P 2	160	3	70	2,970	7.83	3.372	25.4		26.25	58
										24.0		
K.	10/31/34	P 4	55	1	5	1,872	4.03	2.944	43.4*		26.17	..
	11/ 2/34	P 5	127	3	7	1,930	4.72	3.652	45.3*		24.77	..
	11/ 3/34	P 6	116	3	8	1,926	4.26	3.440	47.4*		26.99	53
	11/16/34	P 7	105	3	21	2,266	4.56	2.638	33.9		25.72	37
	11/19/34	P 8	78	2	24	2,304	5.40	2.825	30.7		28.46	33
	11/21/34	P 9	107	3	26	2,322	5.35	3.142	34.4		28.08	38
	11/22/34	P10	125	3	27	2,354	5.73	3.148	32.8		26.61	41
										33.0		
J. M.	12/ 4/34	P11	91	2	14	1,968	5.62	2.691	28.1		27.99	38
	12/ 6/34	P12	73	2	16	2,064	4.70	2.324	29.0		28.22	35
	12/18/34	P18	124	3	28	2,404	6.11	2.654	25.5		28.35	43
										27.5		
C. W.	12/10/34	P13	77	2	3	1,776	4.31	2.637	36.0		27.95	46
	12/12/34	P15	86	2	5	1,754	4.17	2.538	35.7		27.88	44
	12/13/34	P16	116	3	6	1,730	4.35	2.507	33.8		27.74	42
	12/17/34	P17	78	2	10	1,800	4.67	2.462	30.8		28.11	42
	12/31/34	P19	91	2	24	2,214	5.03	2.733	31.8		28.13	46
										33.6		
W.	1/ 8/35	P23	90	2	8	2,210	5.49	2.524	27.0		27.93	39
	1/ 9/35	P24	75	2	9	2,210	5.74	2.443	24.9		28.43	46
	1/22/35	P26	111	3	22	2,560	7.06	3.122	25.9		28.74	47
										25.9		
H. B.	1/ 2/35	P20	91	1	69	2,880	7.01	3.380	28.2		28.38	45
	1/ 3/35	P21	90	2	70	2,820	7.57	3.503	27.1		28.80	44
										27.7		

									21.7			
A. N.	1/16/35	P25	97	2	9	1,816	4.54	2.819	36.3		27.24	52
	1/23/35	P27	126	3	16	1,948	5.12	2.375	27.1		27.59	38
	1/28/35	P28	125	3	21	2,128	5.00	2.397	28.0		27.72	39
	1/29/35	P29	129	3	22	2,136	4.75	2.487	30.8		27.60	35
	2/ 1/35	P31	108	3	25	2,228	5.98	2.724	26.8		27.93	40
	2/ 4/35	P32	114	2	28	2,328	6.30	2.804	26.0		28.22	39
	2/ 6/35	P33	120	2	30	2,330	5.82	2.712	27.3		27.80	35
	2/14/35	P35	75	2	38	2,580	5.88	2.908	29.3		28.52	37
	2/18/35	P36	86	1	42	2,680	6.92	2.930	24.8		28.20	36
	2/19/35	P37	70	2	43	2,720	6.43	3.115	28.4		28.02	45
										28.5		
A.	1/31/35	P30	141	3	7	2,034	5.48	2.684	28.6		27.83	36
										28.6		
B.	3/ 5/35	P39	83	2	34	2,160	5.76	2.786	28.3		28.72	36
	3/ 7/35	P40	94	2	36	2,286	5.94	2.746	27.1		27.60	38
	3/ 8/35	P41	102	2	37	2,386	6.50	3.189	28.8		28.73	41
										28.1		
E. H.	3/15/35	P43	45	1	4	1,560	3.83	2.509	38.4		28.07	36
	3/25/35	P44	46	1	14	1,800	4.43	2.473	32.7		28.08	34
	3/28/35	P45	84	2	17	1,880	5.33	2.569	28.3		28.20	35
	3/29/35	P46	97	2	18	1,940	5.19	2.598	29.3		28.45	32
	4/22/35	P48	118	2	42	2,600	6.53	3.305	29.7		28.81	43
	4/29/35	P49	88	2	49	2,800	6.60	3.646	32.4		28.88	46
	4/30/35	P50	134	3	50	2,880	7.08	3.820	31.6		28.71	50
	5/ 3/35	P51	93	2	53	2,980	7.85	3.534	26.4		28.44	45
	5/ 6/35	P52	64	1	56	2,960	8.52	4.187	28.8		28.23	49
	5/ 8/35	P53	115	3	58	3,000	7.71	3.851	29.3		28.09	44
	5/10/35	P54	68	1	60	3,120	7.95	4.973	36.6		28.21	45
	5/14/35	P55	100	2	64	3,260	8.51	4.879	33.6		28.03	44
	5/15/35	P56	81	2	65	3,300	8.21	4.173	29.8		28.30	43
	5/16/35	P57	77	2	66	3,380	8.32	4.374	30.8		28.32	46
	5/24/35	P58	60	1	74	3,720	10.41	6.139	34.6		28.48	56
										31.5		
								Total average		28.84		
								Standard deviation		2.88		
								Coefficient of variability		10.0%		

* Omitted from averages. High percentages were coincident with high relative humidity of the calorimeter room, the significance of which, as a source of positive error, has been discussed in the text.

cent, the lowest value being 32 (P46). One may reasonably assume, therefore, that the technical error in the observations on infants was probably less than the average of 9 per cent found in the alcohol checks.

RESULTS

The results in terms of averages per hour are presented in table 1. The detailed calorimetric data appeared for all except one infant (H. B.) in the previous paper of this series,[2] in which observations made during

TABLE 2.—*Percentage of Heat Lost in Vaporization in Observations Including Basal Periods and Periods of Activity.*

Subject	Observation Number	Basal Period		Period of Activity*	
		Number of Periods	Percentage	Number of Periods	Percentage
J. M.	P11	1	29.2	1	27.3
	P18	2	26.4	1	23.0
W.	P23	1	28.5	1	26.4
A. N.	P27	2	27.9	1	26.2
	P28	2	27.8	1	28.2
	P29	2	30.3	1	31.1
	P31	1	27.1	2	26.6
	P33	1	26.2	2	27.7
A.	P30	1	31.7	2	28.2
E. H.	P49	1	33.5	1	32.0
	P50	1	35.1	2	31.0
	P51	1	29.5	1	24.4
	P53	2	29.9	1	28.4
	P55	1	32.8	1	34.4
	P56	1	29.2	1	30.9
	P57	1	34.1	1	28.3

*Periods of activity included intervals of sleep. The average increase in basal metabolic rate due to activity was 11 per cent, the maximum being 29 and 28 per cent (P23 and P30).

TABLE 3.—*Average Heat Lost in Vaporization During Basal Periods and Periods of Activity*

	Number of Infants	Number of Observations	Number of Periods	Calories Lost in Vaporization	
				Average, Percentage	Range, Percentage
Basal period.....	9	42	72	29.6	24.0-33.6
Period of activity*.....	6	22	29	27.5	25.2-30.3

* Periods of activity included intervals of sleep.

basal periods only were shown. In table 1 are presented, in addition, observations made during periods which included moderate activity and observations following the administration of thyroxine. The calorimetric data for the latter will appear in a subsequent publication.

The average percentage (weighted) of heat lost in vaporization was 28.8, the range for individual infants being from 24 to 33 (table 1). This average is only slightly higher than that previously found for normal infants (26.5 per cent), marasmic infants (25.6 per cent) and

children and adults (24 per cent).[6] Correction for the error of +9 per cent found in the alcohol checks would lead to an even closer agreement. The range of variation for the ten premature infants (coefficient of variability, 10 per cent) was slightly higher than that found for the ten full term infants on whom observations were previously reported from this laboratory (coefficient of variability, 7.8 per cent).[1b]

The effect of moderate activity on the percentage of heat lost in vaporization of water is shown in tables 2 and 3. In the former, sixteen observations on five infants are presented, in which data on both basal periods and periods including activity were obtained in the same observation. An average augmentation in the basal metabolic rate of 11 per cent and maximum increases of 29 and 28 per cent (P23 and P30, table 2) produced no significant change in the percentage of heat lost by vaporization, the average difference between the loss during basal and that during periods of activity being 2.3 per cent. In table 3 are presented the averages for all basal periods and all periods including activity. The average loss for the individual infants was 29.6 per cent (range, from 24 to 34 per cent) for basal periods and 27.5 per cent (range, from 25 to 30 per cent) for periods of activity. No relationship was observed between the amount of heat lost in vaporization and the augmentation in heat production resulting from activity. Moderate stimulation of the basal metabolic rate of two infants (E. H. and A. N., table 1) by the oral administration of thyroxine produced no appreciable change in the percentage of calories dissipated in vaporization of water.

COMMENT

A systematic investigation of the imbalance in premature infants between the production and the loss of heat, as evidenced by their tendency to a subnormal body temperature, would necessarily include measurements of the relation of heat lost in vaporization of water to total heat production. One might suspect a disturbed relationship between these two physiologic mechanisms, because of the known hydrolability of these subjects, their tendency to edema[7] and the higher water content of their bodies.[8]

The evidence indicates, however, that no such disproportion exists under the conditions of this investigation. The strikingly uniform

6. Levine and Wilson.[1] Soderstrom, G. F., and DuBois, E. F.: Clinical Calorimetry: XXV. The Water Elimination Through Skin and Respiratory Passages in Health and Disease, Arch. Int. Med. **19**:931 (May) 1917.

7. Ylppö, A.: Pathologisch-anatomische Studien bei Frühgeborenen, Ztschr. f. Kinderh. **20**:212, 1919. Eckstein, A., and Schumacher, H. M.: Untersuchungen über das Sklerödem der Frühgeborenen, ibid. **54**:338, 1933.

8. Langstein, L., and Edelstein, E.: Die chemische Zusammensetzung frühgeborener Säuglinge u. ihr Wachstumansatz, Ztschr. f. Kinderh. **15**:49, 1917.

relationship between heat production and the loss of heat in vaporization of water which exists from early infancy to old age under standard conditions of calorimetry applies also to premature infants.

SUMMARY AND CONCLUSIONS

The elimination of water through the skin and respiratory passages and the heat production of ten premature boys ranging in age from 3 to 64 days and in weight from 1,560 to 2,870 Gm. at the time of the first observation was studied in fifty-one calorimetric observations of from three-fourths to two and one-half hours. Under standard conditions of indirect calorimetry and with the temperature and the relative humidity in all observations ranging between 26 and 29 C. and 30 and 60 per cent, respectively, the average heat lost in vaporization represented 29 per cent of the total heat production, the extreme figures for individual infants being 24 and 33 per cent. These figures closely parallel the average of 26 per cent found for normal and marasmic infants and that of 24 per cent found for adults and children. Moderate augmentation of the basal metabolic rate by activity or thyroxine caused no significant change in the percentage of heat lost in vaporization.

These calorimetric studies furnish no evidence of a disturbance in the mechanism of loss of heat by vaporization to explain the tendency for subnormal body temperatures to develop in premature infants.

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ALLERGIC ABDOMINAL PAIN IN CHILDREN

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Pain in the abdomen is a common complaint in children. Frequently the cause of the pain cannot be determined, as investigation is usually uninformative.

Lust [1] described abdominal pain, particularly the type localizing about the umbilicus ("navel colic"), as common among children. Moro [2] also depicted recurrent navel colic. Both writers mentioned the difficulty of ascertaining the cause of the condition and the paucity of objective findings.

Food allergy as a cause of abdominal pain has been emphasized by several investigators (Bray,[3] Rowe,[4] Laroche and his co-workers,[5] Duke,[6] Andresen,[7] Rackemann,[8] Hollander,[9] Alexander [10] and Lintz [11]). Occasionally, in these studies it has been shown that abdominal pain of obscure origin followed the eating of certain foods, that the pain disap-

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1. Lust, F.: Diagnostik und Therapie der Kinderkrankheiten, ed. 7, Vienna, Urban & Schwarzenberg, 1932, p. 177.

2. Moro, E., in von Pfaundler, M., and Schlossman, A.: Handbuch der Kinderheilkunde, ed. 5, Leipzig, F. C. W. Vogel, 1910, p. 19.

3. Bray, G. W.: Recent Advances in Allergy, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1934, p. 390.

4. Rowe, A. H.: Food Allergy, Philadelphia, Lea & Febiger, 1931.

5. Laroche, G., and others: Alimentary Anaphylaxis, Berkeley, Calif., University of California Press, 1930.

6. Duke, W. W.: Food Allergy as a Cause of Abdominal Pain, Arch. Int. Med. **28**:151 (Aug.) 1921.

7. Andresen, A. F. R.: Gastrointestinal Manifestations of Food Allergy, M. J. & Rec. **122**:271, 1925.

8. Rackemann, F. M.: The Importance of Foreign Proteins and Other Foreign Substances in the Etiology of Disease, Internat. Clin. **1**:56, 1922.

9. Hollander, E.: Mucous Colitis Due to Food Allergy, Am. J. M. Sc. **174**: 495, 1927.

10. Alexander, H.: Localized Allergy, M. Clin. North America **11**:399, 1927.

11. Lintz, W.: The Diagnosis and Treatment of Two Hundred and Twenty-Five Cases of Gastro-Intestinal Allergy, New York State J. Med. **34**:282 (April 1) 1934.

peared on withdrawal of these foods and that positive cutaneous reactions to extracts of these ingestants could be demonstrated. Such a triad fulfils in general the required criteria of allergy.

Sir William Osler,[12] in a series of papers dating from 1895 onward, described a group of patients with purpura, urticaria and angioneurotic edema who in addition had gastro-intestinal symptoms. A large proportion of these patients had suffered from abdominal colic with occasional vomiting and diarrhea. In one publication, Osler called attention to the surgical aspect of this condition, stating that it was similar to appendicitis but distinguished from it by the presence of cutaneous lesions. However, a few of the patients had attacks of abdominal pain without any simultaneous outbreak of cutaneous lesions. In 1914, Osler [13] mentioned the similarity between such a condition and that exhibited by patients who suffered from hypersensitiveness to shellfish or from hay fever. He mentioned also the relationship of serum rashes to the condition that he described and stated that his patients might well be presenting "anaphylactic" phenomena. In Laroche's monograph it was noted that guinea-pigs and other animals can be actively sensitized by the feeding of eggs or milk. This phenomenon was previously described by Rosenau and Anderson.[14] Alexander and Eyermann [15] have observed patients with abdominal pain who in addition manifested urticaria or purpura. The striking similarity between abdominal symptoms of food allergy and those of Henoch's purpura suggested to Alexander and Eyermann a common etiologic factor, since a diet eliminating certain foods caused the disappearance of symptoms. Yet cutaneous tests showed no significant reactions to these foods.

The mechanism of abdominal symptoms is conjectural. The simultaneous occurrence of "visceral hives" and manifestations on the skin has been confirmed by the finding at operation of local areas of edema

12. Osler, W.: On the Visceral Complications of Erythema Exudativum Multiforme, Am. J. M. Sc. **110**:629, 1895; On the Visceral Manifestations of the Erythema Group of Skin Diseases, Tr. A. Am. Physicians **18**:599, 1903; On the Visceral Manifestations of the Erythema Group of Skin Diseases, Am. J. M. Sc. **127**:1, 1904; On the Surgical Importance of the Visceral Crises in the Erythema Group of Skin Diseases, ibid. **127**:751, 1904.

13. Osler, W.: The Visceral Lesions of Purpura and Allied Conditions, Brit. M. J. **1**:517, 1914.

14. Rosenau, M. J., and Anderson, J. F.: A Study of the Cause of Sudden Death Following the Injection of Horse Serum, Bulletin 29, United States Public Health Service, Hygienic Laboratory, 1906.

15. Alexander, H. L., and Eyermann, C. H.: Food Allergy in Henoch's Purpura, Arch. Dermat. & Syph. **16**:322 (Sept.) 1927; Allergic Purpura, J. A. M. A. **92**:2092 (June 22) 1929. Eyermann, C. H.: Allergic Purpura, South. M. J. **28**:341, 1935.

or giant urticaria in the wall of the bowel. Bray [16] stated the belief that the absorption of undigested protein into the blood through the normal or impaired mucous membrane of the intestinal tract causes sensitization of the cells to these nocuous whole proteins. When these proteins are absorbed on future occasions a reaction takes place—the allergic reaction—causing increased capillary permeability, edema or spasm of the smooth muscles. Such a reaction may take place as a result of direct contact between the specific food and the gastro-intestinal mucous membrane (contact reaction), or the allergic reaction may result in the intestinal tract after absorption of the food into the general circulation (general reaction). These phenomena may explain the immediate and delayed onset of abdominal pain after ingestion of a specific food.

The purpose of this paper is to discuss manifestations in children of abdominal symptoms which seem to be of allergic origin. The abdominal symptoms and pathologic changes are less readily thought of as an allergic reaction than the more frequent manifestations in the lungs, nose and skin. We have seen instances in which abdominal symptoms occurred in children for years until an attack of urticaria or angioneurotic edema gave a hint as to the etiology. Yet food allergy should be suspected in children. The frequent occurrence of common food allergens in the child's diet, the forcing of food, the appearance of a symptom during the first decade, when allergic symptoms first become prominent, and the diminution of symptoms with advance in age (spontaneous loss of sensitivity?) make it reasonable to presume that these abdominal symptoms are allergic. Moreover, in children the rather frequent association of abdominal pain with manifestations such as asthma, urticaria and angioneurotic edema suggests that this pain may often be allergic.

Studies of the blood of our patients showed no particular characteristics. Eosinophilia was occasionally demonstrable. The leukopenic index [17] unfortunately was not determined. In such studies, foods which produce allergic symptoms are capable of depressing the total leukocytic count.

According to Gay,[18] food allergens used as a gastric test meal have the ability to depress or to inhibit totally the secretion of free hydrochloric acid, while nondamaging foods are followed by a normal

16. Bray, G. W.: Food Allergy, M. Press & Circ. (supp.) **189**:x (July 25) 1934.

17. Vaughan, W. T.: Food Allergens: III. The Leukopenic Index, J. Allergy **5**:601, 1934; Further Studies on the Leukopenic Index in Food Allergy, ibid. **6**:78, 1934.

18. Gay, L. P.: Gastro-Intestinal Allergy: IV. The Leukopenic Index as a Method of Specific Diagnosis of Allergens Causing Peptic Ulcer, J. A. M. A. **106**:969 (March 21) 1936.

response. We made no such tests because of the obvious difficulty which might be encountered when extracting the stomach contents in the presence of abdominal pain produced by pain-producing foods. However, we have performed a series of fractional gastric analyses employing Cheney's [19] alcohol meal. We found that the response of acid gastric secretion in the majority of our patients was below the average normal found in an equal number of control patients.

Eyermann [20] described roentgenographic findings of intestinal hyperperistalsis in a patient with severe abdominal pain caused by ingested food. Fluoroscopic studies by Rackemann [21] of a severely asthmatic patient revealed a definite spasm of the pylorus, which disappeared, however, between attacks. In our patients were frequently found roentgenographic evidence of disturbance in physiologic function of the gastro-intestinal tract with the use of an ordinary barium sulfate meal—and of more pronounced dysfunction when the specific food was added to the meal. These findings were mainly (1) spasm of the pylorus, (2) delayed emptying of the stomach and (3) hypertonicity and hyperperistalsis of the intestine. The last was a characteristic finding.

Cutaneous tests (intradermal, scratch and passive transfer methods) have not been helpful. Occasionally the causative food has been demonstrated or confirmed by a positive cutaneous reaction. However, in the majority of our cases these tests have offered no clue, and in some instances they have not been confirmatory when the food allergens have been proved clinically. Delayed cutaneous reactions were also of no significance. The absence of cutaneous reactions in our patients may be due to the fact that, as Walzer [22] pointed out, there are so many clinical forms of hypersensitiveness to food which are not based on a reagin mechanism. Consequently, the cutaneous reactions are negative because of the absence of reagins in the skin. Gay,[18] on the other hand, expressed the opinion that cutaneous tests on patients with gastrointestinal allergy are of little value because the clinical reactions of the allergens are of the cumulative type. Vaughan [23] suggested that this might be because only certain tissues of the body (intestinal tract) are sensitive while others (skin) are not.

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19. Cheney, G.: A Simplified Method of Gastric Analysis, Am. J. M. Sc. **177**:110, 1929.

20. Eyermann, C. H.: X-Ray Demonstration of Colonic Reactions in Food Allergy, J. Missouri M. A. **24**:129, 1927.

21. Rackemann, F. M.: Clinical Allergy: Asthma and Hay Fever, New York, The Macmillian Company, 1931, p. 571.

22. Walzer, M., in Coca, A. F.; Walzer, M., and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, Publisher, 1931, p. 413.

23. Vaughan, W. T.: Food Allergens: II. Trial Diets in the Elimination of Allergenic Foods, J.Immunol. **20**:313, 1931.

For the sake of convenience, in the subsequent discussion abdominal pain is classified and described under three arbitrary divisions, depending on severity.

SEVERE ABDOMINAL PAIN SIMULATING AN "ACUTE SURGICAL ABDOMEN"

We have seen abdominal symptoms of violent nature which could easily have been mistaken for those caused by an abdominal lesion requiring surgical operation. This experience suggested a review of a fairly extensive series of pediatric surgical histories from our hospital records. Forty instances were found in which children who were admitted with the chief complaint of abdominal pain and whose condition was initially diagnosed as a surgical emergency were discharged without surgical intervention. One fourth of these (ten patients) appeared to be of allergic constitution.[24] Their records included most or all of the following characteristics: (1) a family history of allergy; (2) a past history of some type of allergy; (3) a previous history of gastro-intestinal symptoms or specific food sensitivities; (4) eosinophilia, and (5) on admission to the hospital a complaint of severe abdominal pain with atypical or negative findings on physical examination of the abdomen. The following case histories are examples:

CASE 1.—P. L. was aged 9 years on admission to the hospital. The maternal grandmother had asthma and hay fever; a maternal uncle had hay fever, and the paternal grandmother had asthma. The child had recurrent "hives" in early childhood. For the month preceding admission to the hospital there had been abdominal cramplike pain of a few minutes' duration about the umbilical region. More recently the attacks of pain had occurred daily, lasting one-half hour or longer, and had been associated with vomiting and frequent bowel movements. On the day of admission to the hospital the patient was seized with severe abdominal pain, nausea and vomiting. The physical findings seemed insignificant except that the colon could be palpated as an elongated, mobile, nontender mass in the right lower quadrant and as a smaller mass in the left lower quadrant. On the following day, these fantom tumors disappeared, and subjective symptoms subsided. The white blood cell count on admission was 12,500, with 70 per cent neutrophilic leukocytes and 6 per cent eosinophilic leukocytes. A roentgenogram made after a barium clysma showed exaggerated haustral markings in the cecum and ascending colon. A urogram showed the kidneys to be apparently normal in function and morphology. However, shortly after intravenous administration of the dye (neo-iopax) generalized urticaria and pruritus appeared, which were relieved by the administration of epinephrine. No further attacks of pain were noted during the period of hospitalization.

Pain occurring as a pronounced symptom of hypersensitiveness to food has not been rare in our experience. The true cause of pain may be overlooked, and in some cases this oversight has been a reason for surgical intervention.

24. Further study is being made of these patients.

Such a case actually encountered by us is cited.

CASE 2.—P. G. when admitted to the hospital was 6½ years of age. No history of allergic manifestations in the immediate family could be elicited. The child was breast fed from birth until the age of 3 months, when a relief feeding of cow's milk was given, whereupon a severe attack of vomiting and colic ensued. Repeated attempts to feed cow's milk invariably provoked a similar reaction. The child was weaned at 11 months with the utmost difficulty, for it vomited after each ingestion of milk. Small, repeated feedings of milk were given under a physician's advice in order to develop tolerance. Milk was entirely discontinued at 2 years of age, after the child had repeatedly shown inability to ingest even small amounts. An eczematoid rash appeared on the face when the patient was 3 months of age; later it spread to the trunk, and it had persisted since. When the child was 14 months of age, after "unresolved pneumonia," asthmatic attacks began, and these had recurred since that time with increasing frequency and intensity.

The patient was admitted to the hospital with a history of recurrent attacks of cramplike umbilical pain for eight months. The mother noted that these attacks frequently followed ingestion of pineapple juice. Four days prior to admission the patient had periumbilical pain, nausea, vomiting and fever. The pain finally localized in the right lower quadrant.

Study of the blood showed white blood cells 17,900, polymorphonuclear neutrophils 86 per cent, lymphocytes 12 per cent and monocytes 2 per cent. No eosinophils were reported.

Physical examination revealed a generalized eczematoid induration of the skin, with numerous scratch marks. Examination of the abdomen revealed rigidity of the right rectus muscle, marked tenderness over McBurney's point and rebound tenderness. A diagnosis of acute appendicitis was made by two attending surgeons. Appendectomy was performed.

Gross and microscopic examination of the appendix revealed normal structure.

Cutaneous tests (indirect method, the father being used as subject) elicited marked positive reactions to milk, almond, mustard and salmon and slight reactions to wheat, beef, lamb, pork, peanut, herring, apple, green pea, string bean, carrot and silk. The reactions to pineapple, prunes and many other foods were negative.

Since discharge from the hospital, the patient has had recurrences of abdominal pain, always about the navel, occurring three or four times weekly and lasting from one-half to one hour. Experimentally, small amounts of pineapple juice or prune juice induce pain in the abdomen five minutes after ingestion. Traces of mustard produce marked swelling and blistering of the lips. (The mother stated that these foods had inadvertently been given prior to the attack which preceded hospitalization.) A fractional gastric analysis (alcohol meal) revealed low free and total acidity in all specimens.

ABDOMINAL PAIN OF SUBACUTE RECURRENT NATURE

Subacute recurrent abdominal pain is frequent in children, especially in those manifesting an allergic condition. Occasionally the diagnosis of chronic appendicitis, pyelitis or some other type of gastro-intestinal disease is made.

Detailed inquiry has made us suspect the allergic nature of this type of complaint. In many patients the history of allergy in the family

placed this abdominal pain symptom complex under suspicion of hypersensitiveness. It was found that foods might be the etiologic factor since examples have been encountered in which specific foods caused abdominal pain after ingestion. Food dislikes have incriminated certain foods which, when intentionally forced, produced abdominal pain. In some instances pain followed shortly after the introduction of a new food into the child's diet. Many of the patients had a history of frequent colic and vomiting during infancy or early childhood, which could be interpreted as signs of food allergy.

The location and nature of the pain are fairly characteristic. Although localization is not as accurate as in the adult, the child usually points to the region of the umbilicus. Occasionally, the epigastrium, paraumbilical regions or right lower quadrant is designated. Pain is usually described as cramplike. The duration of these bouts of pain varies between minutes and hours, and they may occur one or more times a day or at intervals of weeks, months or longer periods. As a rule, there are other associated gastro-intestinal symptoms, such as constipation, diarrhea, flatulence, mucous or watery stools, nausea or vomiting. Frequently the pain occurs after eating. Urticaria may appear concurrently with the attacks of pain. Generally there is no fever.

On physical examination of the abdomen, usually no abnormal findings are elicited. Localized tenderness may be present during the attack but is frequently absent. Occasionally one can palpate the outlines of the colon.

A careful history has been most helpful. Idiosyncrasies in eating or dislikes for particular foods have often served as clues. Subsequently simple diets were instituted in which the suspected foods were avoided.

If the symptoms cleared up, we confirmed our diagnosis with a "forced trial" diet, by which it was hoped to exceed the nonallergic threshold or tolerance and thus reproduce the clinical symptoms. This approach has been very useful. The following printed instructions were given to the parent.

1. Choose a time when the child is perfectly free from symptoms.

2. Give the suspected food in large amounts, morning, noon and evening (and even between regular meals). Give it in all forms (raw, cooked or baked, alone or mixed with other foods).

3. With the onset of symptoms, discontinue the food. Symptoms usually appear in from four to twenty-four hours (sometimes sooner or later). Only one suspected food should be tested at a time.[25]

25. Such a test might seem inconclusive because it could be argued that ordinarily the child does not consume the suspected food in the large quantities which might be administered in this trial diet. Actually, the amount of the specific food reported in "positive" trials was impressively small, so that quantity could not be presumed as the cause of symptoms.

CASE 3.—M. K. was admitted to the hospital at the age of 6 years, with a history of allergy in the immediate family. The child had had attacks of vomiting and diarrhea since it was 2 years of age. These attacks occurred about six times yearly, persisted from one to two weeks and were usually associated with severe abdominal pain. These periodic episodes were characterized by complete intolerance to food, loss of weight, "rings under the eyes" and frequent loose, mucous stools. Occasionally blood was noted in the stools.

During the patient's infancy cow's milk was fed with difficulty and frequently induced vomiting. Milk, eggs and cereals had always been disliked. Urticarial rashes and transient swelling of the eyelids had been noted since the child was 4 years of age.

A differential white blood cell count revealed eosinophilia (15 per cent). A fractional gastric analysis revealed no free hydrochloric acid and low total acidity. Examination of the stools and urine and tuberculin tests of the skin gave negative results. Cutaneous tests with protein showed the patient to be sensitive to milk, egg, lamb, beef, dust, goat hair and feathers. Forced trial feeding with milk induced abdominal pain, vomiting and mucous stools. A similar trial with egg was impossible because the child absolutely refused this food. Forced trial feeding with beef induced nausea and vomiting.

For a period of five months the child was not offered these reaction-eliciting foods and was given hydrochloric acid by mouth. During this time no similar episodes occurred. For the past year medication has been discontinued and a complete diet instituted. Occasional recurrences of abdominal pain are reported when more than minimal amounts of milk and egg are ingested.

ABDOMINAL PAIN AS A MINOR SYMPTOM

Abdominal pain may appear as a minor symptom during an acute attack of asthma and may occur more often during severe outbreaks of urticaria or angioneurotic edema. Rarely, the pain ushers in the attack; more commonly, it appears concurrently. Abdominal pain is seldom complained of by the patient since the major symptomatology obscures it.

CASE 4.—R. C., aged 11 years at the time of admission to the hospital, had been subject to recurrent attacks of urticaria since the age of 6 years. Round, irregular red patches with white raised centers appeared on the trunk and extremities almost daily during the summer. From the age of 7 years the patient had had frequent large, tense swellings of the eyes, lips, tongue, soles of the feet and dorsa of the hands. A paternal cousin had similar swellings of the eyes and face and urticarial eruptions which were traced to ingested sea food.

For the month preceding the initial observation attacks of severe cramplike umbilical pain had been noted, immediately followed by an urticarial eruption. The pain caused the child to "double up" and feel nauseated, and it disappeared, as a rule, with the appearance of the rash. The mother noted that the swellings followed the ingestion of tomato and catchup.

All cutaneous tests, including those made with tomato extract, were negative.

Experimentally, 2 or 3 teaspoonfuls of tomato, tomato juice or catchup induced edema of the eye (or some other part of the body) and urticarial wheals within twelve hours. This has been confirmed on several occasions.

TREATMENT

Various forms of therapy have been tried. Severe acute attacks of abdominal pain have been successfully controlled by gastric lavage and enema, although we have rarely had occasion to resort to these procedures. We have had one experience with the hypodermic use of epinephrine in excellently controlling a severe acute attack.

Elimination of Offending Food.—This is the ideal therapy. However, in some instances no clue is offered by the history, the cutaneous reactions or "trial diets." Again, there may be such a multiplicity of causative foods as to make it impracticable to avoid them all.

Oral Desensitization.—This has not been successful in our experience.

Acid Therapy.—In a number of cases in which gastric analysis revealed hypochlorhydria or achlorhydria, it seemed that hydrochloric acid might be of benefit. Actually, this therapy was found to be the most useful of all tried. We used dilute hydrochloric acid (U. S. P.) in doses of at least ½ to 1 drachm (2 to 4 cc.) three times a day in fruit juice (sweetened if desired) or in cold water.

Desiccated Hog's Stomach.—A preparation of stomach U. S. P.[26] was tried but with no significant benefit. The oral administration of this preparation, according to Schiff and Tahl,[27] will stimulate the gastric secretion of free hydrochloric acid.

Antispasmodics.—Belladonna and atropine have been recommended. In our experience they have been of doubtful value.

Catharsis.—In view of the frequency of constipation as an associated complaint, we have tried small doses of a mild cathartic as routine medication. The results have not been encouraging.

Ephedrine.—We are using this drug in small repeated doses since it is reputed to influence allergic reactions. We have not yet had enough experience to evaluate it in controlling abdominal symptoms.

Follow-up of untreated patients shows, as a rule, progressive diminution of symptoms. Frequently the pain disappears spontaneously before the age of puberty.

SUMMARY AND CONCLUSION

1. Abdominal pain of allergic origin may arbitrarily be classified in three types: (*a*) severe abdominal pain simulating an "acute surgical abdomen"; (*b*) abdominal pain of subacute recurrent nature; and (*c*)

26. Ventriculin was used, furnished by Parke, Davis & Co.

27. Schiff, L., and Tahl, T.: The Effects of Desiccated Hog's Stomach in Achlorhydria, Am. J. Digest. Dis. & Nutrition **1**:543, 1934.

abdominal pain as a minor symptom. Cases illustrating each of these types were described.

2. The allergic nature of these complaints may be proved by history and "trial diets."

3. Since symptoms of food allergy may imitate those of a surgical lesion in the abdomen, such symptoms occurring in allergic persons or members of allergic families should be evaluated with this point in mind.

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EFFECT OF THYROID THERAPY ON THE MENTAL AND PHYSICAL GROWTH OF CRETINOUS INFANTS

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Approximately eighteen centuries ago Galen described the thyroid gland. One century ago Cooper experimentally removed the gland from a dog. Sixty years ago myxedema was described, and forty years ago thyroid juice was injected subcutaneously as a cure. Twenty years ago Kendall isolated and synthesized thyroxine. Thirty years ago a German compiled a tome listing the books, monographs and papers on the subject of cretinism—a total of 2,468 titles. Since then the literature has expanded enormously.

Among all the reports of investigations there is none of a detailed objective study of the effect of thyroxine on early mental growth. These effects are truly remarkable. The aim of this paper is to describe their nature, to show the relationships between psychologic and physical factors and to indicate the diagnostic significance of the behavior changes produced by thyroid therapy.

It is commonly asserted that the early diagnosis and treatment of cretinism are highly important in effecting a good therapeutic response. It is almost as commonly stated that many cretins respond poorly to treatment even when it is promptly given and, conversely, that the results of treatment are sometimes surprisingly good even after a delay of several years. This variation in the effects of thyroid therapy is ascribed to such causes as inadequate treatment, differences in the severity of the thyroid deficiency, involvement of other endocrine glands and underlying primary mental deficiency. Tredgold[1] said: "The general experience that a number of cretins show no mental improvement under treatment, although the physical signs disappear, leads me to think that there are probably two distinct types of cretins. In one type the mental and physical retardation are clearly due to hypothyroidism,

From the Clinic of Child Development and the Department of Pediatrics, Yale University School of Medicine.

1. Tredgold, A. F.: Mental Deficiency (Amentia), ed. 5, New York, William Wood & Company, 1929, p. 274.

and the child becomes normal under treatment. In the other type I am disposed to think that the essential condition is one of primary amentia, the hypothyroidism being a superadded complication."

Whatever the factors behind this difference in response to treatment are, the distinction between the two types of cretinism is real, and a method of early differentiation and prognosis is needed. Just how good the best results are is another disputed subject, some investigators granting complete normality and others asserting that normality is never fully achieved.

The physical and mental expressions of the infant's growth cannot, of course, be sharply separated. They are fundamentally one. In this paper we present physical and mental findings in close association. We formulated the mental findings quantitatively by using the Yale norms of infant development. Extensive cinema records also served to place the data on mental growth on an objective and quantitative basis.

REPORT OF CASES

We have assembled data on six cases of cretinism or hypothyroidism in which the condition was recognized and adequately treated in infancy.[2] Each patient is designated by an initial preceded by a number giving the age in weeks at which treatment with thyroid was begun. As cretinism occurs with much greater frequency in girls, it is not surprising that all six patients were girls. For purposes of comparison and control we included data on O-C, an adult male cretin untreated in childhood, and O-N, a normal infant girl. Figure 1 shows the cretins who are under consideration. All the infants were photographed before treatment was begun with the exception of 27-M and 80-H.

CASE 1.—Patient 36-A was the eighth child of a large Italian family. Seven older and two younger siblings were living and well. Labor was induced at term because of signs of toxemia. The weight at birth was 6¼ pounds (2,835 Gm.). The physical examination at birth gave negative results except for a recorded impression of immaturity. The neonatal course of development was uneventful. The child was discharged on the tenth day, and a note was made that the abdomen was tense and prominent. When 3 months of age she was readmitted to the hospital, with vomiting and diarrhea. Physical examination showed dehydration, subnormal temperature, otitis media, conjugate movements of the eyes, a full, tense abdomen and unresponsiveness. During the subsequent weeks the

2. Dr. Ethel Dunham, lecturer on clinical pediatrics, referred 27-M to us and made her own early records of the case available. Miss Elizabeth E. Lord and Mr. Burton M. Castner, of The Yale Clinic of Child Development, secured and analyzed the data on behavior in this case. Mr. George L. Seth, research fellow, assisted in the cinema analysis of several cases. Dr. A. S. Brown, of Waterbury, Conn., cooperated in the study of 80-H. Dr. Charles LaMoure, superintendent of the Mansfield Training School and Hospital, helped us to secure the follow-up data on O-C.

classic characteristics of cretinism appeared. A diagnosis of cretinism was made when the patient was 32 weeks old. Treatment began when she was 36 weeks old, with desiccated thyroid gland; a dose of 1 grain (0.064 Gm.) daily, later increased to 2½ grains (0.16 Gm.) daily, was well tolerated. At the time of writing the child is 2½ years old.

CASE 2.—Patient 46-S, of Irish extraction, was a fourth child. Two siblings were alive and well, and one sibling had died at birth, the cause of death being unknown. Both parents were alive and well. The birth and neonatal history were normal. The weight at birth was 10 pounds and 11 ounces (4,848 Gm.). At about 6 months the following symptoms were noted: a large abdomen, a protruding tongue, constipation and slowness of growth. A diagnosis of cretinism was made when the child was 40 weeks old. Treatment began when she was 46 weeks old, with desiccated thyroid gland; 1 grain daily was given at first, and

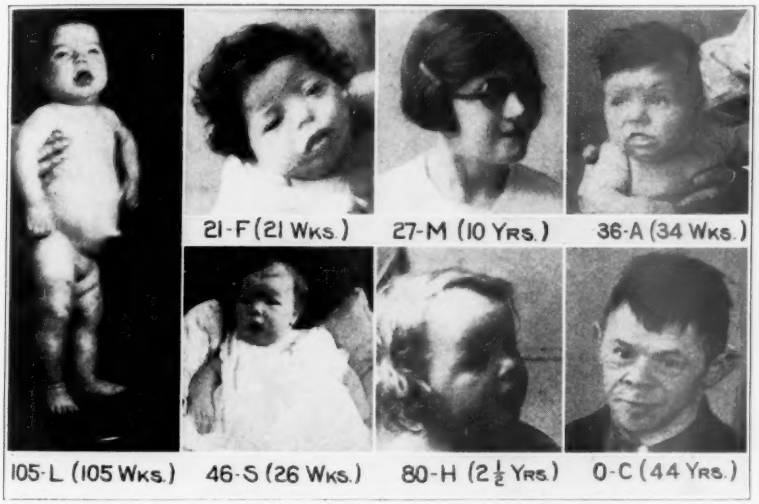

Fig. 1.—The six children who received thyroid therapy and a cretin (O-C) who did not. Patients 27-M and 80-H are shown after therapy; the others, before.

the dose was increased to 1½ grains (0.096 Gm.) daily. Larger doses were not tolerated. At the time of writing the child is 3 years old.

CASE 3.—Patient 27-M was a first-born child; two younger siblings were alive and well. The mother had enlargement of the thyroid isthmus without signs of thyroid dysfunction. The birth and neonatal history were normal. The weight at birth was 8¼ pounds (3,742 Gm.). A diagnosis of cretinism was made when the infant was 27 weeks old. Treatment consisted at first of the administration of 1 grain of thyroxin daily; the dose was increased to from 4 to 6 grains (0.25 to 0.38 Gm.) daily. Signs of intolerance were shown when the larger doses were given. At 10 years of age the patient was taking 2 grains (0.12 Gm.) daily.

CASE 4.—Patient 105-L, of Austrian extraction, was a third child; two siblings and both parents were alive and well. The weight at birth was 6½ pounds (2,948 Gm.). The birth was normal, but the cretin facies was present from birth. A diagnosis of cretinism was not made until the patient was 2

years of age. Treatment consisted of the administration of desiccated thyroid gland; a dose of ¼ grain (0.0016 Gm.) daily was increased soon to 1½ grains (0.096 Gm.) and later to from 3 to 5 grains (0.19 to 0.32 Gm.) daily. The large doses were well tolerated. On one occasion, when 15 grains (0.96 Gm.) was taken, the child showed some irritability. At the time of writing she is 10 years of age.

CASE 5.—Patient 21-F was the ninth child of an Italian family. Seven siblings were alive and well; another sibling had died of the results of an accident. Both parents were alive and well. The weight at birth was 12 pounds (5,443 Gm.). The birth itself was normal, but physical examination showed maldevelopment of the left nostril, a coloboma of the left iris and a dermoid cyst in the lower nasal quadrant of the cornea. The neonatal development was relatively normal. The child was readmitted to the hospital at the age of 5 months because of enlargement of the abdomen and deformity of the nose and one eye. A diagnosis of cretinism was made when she was 21 weeks old. Treatment consisted of the administration of 1 grain (0.064 Gm.) of desiccated thyroid daily. An increased dose was not tolerated. At the time of writing the child is 18 months old.

CASE 6.—Patient 80-H was a fourth child. Two siblings were alive and well and one sibling had died at the age of 6 years, of spina bifida and hydrocephalus. Both parents were alive and well. The birth was normal, but general development was retarded. A diagnosis of cretinism was made when the child was 17 months old. Treatment consisted of the administration of desiccated thyroid substance; 1½ grain (0.096 Gm.) was given daily at first, and this dose was increased to 8 grains (0.51 Gm.) with no untoward effect. The child was taking 1 grain daily and was doing well at the age of 3 years.

Table 1 shows a summary of the data for each case. The range of findings was wide. Mental retardation, as measured by the developmental quotient (the ratio between the diagnostic behavior age level and the chronological age), ranged from 10 to 85 points below 100. Improvement in mental status ranged from 15 to 65 points. The duration of therapy at the time of writing has been from one to ten years.

At the time of the first examination, or early in the course of treatment, in each case, a clinical estimate of the prognosis was made. For one half of the patients defective development was predicted; for the other half the outlook appeared favorable. On this basis the patients are arranged in pairs. In the case of 21-F, the improvement was far greater than was expected. In two cases, therefore, the mental status remained defective, while in four it improved until it was within the normal range. We have been lenient in our application of the term normal and have applied it to all the patients who were lifted definitely above the zone of mental deficiency. If the word normal is construed as signifying average intelligence, 46-S is the only child who can be so described.

Figure 2 pictures an adult (O-C), to remind one of the fate of the untreated cretin. This patient was first examined (by A.G.) when he was 20 years of age. At that time his behavior level, or mental age, was approximately 6 years. Twenty-four years later, when he was

44 years of age, his behavior level remained the same. On numerous tests of judgment, drawing, memory span, counting and comprehension he showed almost unaltered the behavior patterns which he exhibited when he was just out of his teens. During the previous six years he had lived in a training school. Thyroid treatment had been attempted, but it was so poorly tolerated that it was not continued. He became irritable and lost weight while taking 1 grain a day. In this connection one may raise the question whether such a degree of tolerance is compatible with a diagnosis of cretinism. It is possible, however, that the

TABLE 1.—*Summary of Data for the Six Patients* *

Patient	105-L	27-M	36-A	46-S	21-F	80-H	O-C	O-N
Sex	F	F	F	F	F	F	M	F
Maternal history	Irrelevant	Adenoma of the thyroid	Pre-eclampsia	Irrelevant	Irrelevant	Irrelevant	.....	Irrelevant
Siblings	N	N	N	N	N	Spina bifida	Dementia praecox	N
Order of birth	3	1	8	4	9	3	4	2
Weight at birth	N	N	Under	Over	Over	Over	.....	N
Age at first examination	24 mo.	6 mo.	3 mo.	10 mo.	5 mo.	19 mo.	19 yr.	1 mo.
Age at last examination	9 yr.	10 yr.	30 mo.	36 mo.	18 mo.	36 mo.	44 yr.	5 yr.
Roentgen findings	+	+	+	+	+	—	—	—
Physical measurements	+	+	+	+	+	+	+	+
Behavior examinations	7	22	10	9	7	4	2	21
Cinema records	1	3	8	8	7	3	1	20
Age at which thyroid therapy was begun	105 wk.	27 wk.	36 wk	46 wk.	21 wk.	80 wk.	38 yr.	..
Duration of therapy	7 yr.	10 yr.	94 wk.	110 wk.	59 wk.	81 wk.	0	0
Original prognosis	D	N	D	N	D	N	D	N
Original developmental quotient	25	15	40	60	45	50	40	100
Gain in developmental quotient	15	65	20	40	30	25	0	..
Developmental quotient attained	45	80	60	90	75	75	40	100
Mental status	D	N	D	N	N	N	D	N

* D indicates defective; N, normal.

reaction of the organism to thyroid substance is affected by hypothyroidism of long standing, which in itself is competent to alter the total biochemical complex. To what extent thyroid therapy in infancy would have elevated the level of behavior one can conjecture, but one must do so with caution.

COMPARISON OF 36-A AND 46-S

Patients 36-A and 46-S may profitably be compared in detail. The dissimilar effect of thyroid on their physical and mental characteristics is particularly noteworthy. Patient 36-A came under our observation at the age of 15 weeks and was reexamined at 20 weeks and again at 32 weeks. From the first, serious mental retardation was recognized and cretinism was suspected. Circumstances caused a delay in therapy, and during that time the classic signs of cretinism emerged.

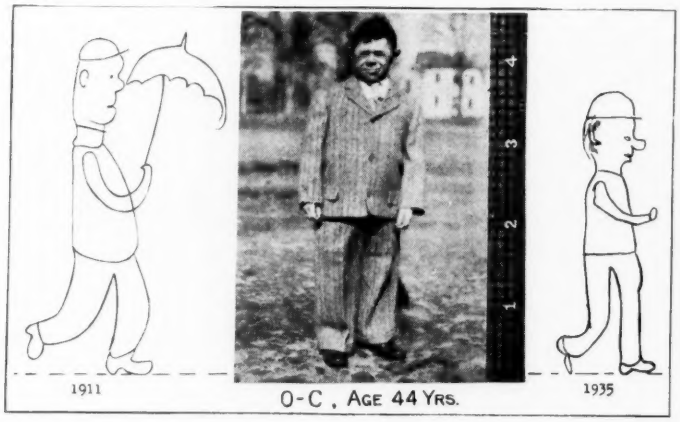

Fig. 2.—An untreated cretin (O-C) at the age of 44 years, with two of his drawings, one made when he was 20 and the other when he was 44. The scale shows the size of the drawings in inches and of the cretin, approximately, in feet. At 44, O-C was 4 feet tall.

Fig. 3.—Patient 36-A, before and after she received thyroid therapy.

until, when the child was 32 weeks old, the diagnosis was obvious. Treatment began when she was 36 weeks of age. Figure 3 shows the marked physical improvement after forty-two weeks of thyroid treatment. Mentally, however, the child remained defective.

Figure 4 shows 46-S after forty weeks of treatment. Therapy was begun ten weeks later than with 36-A, though it is evident that a diagnosis was possible many weeks earlier. Indeed, the portrait photographer might have made the diagnosis when the child was 6 months old! Her physical improvement was as striking as that of 36-A; her mental improvement, far greater. We regarded her as normal, in spite of the severe mental retardation (50 per cent) which she showed at the age of 40 weeks, when she might have been classified as of imbecile intelligence.

Diagnostic Signs.—When treatment was begun both infants showed that unmistakable composite of clinical signs which constitutes cretinism. These distinctive characteristics, physical and mental, are mutually related, yet each retains

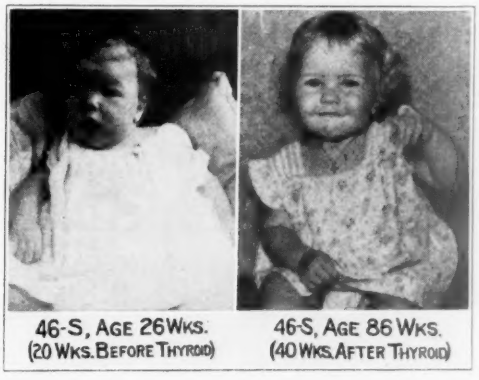

Fig. 4.—Patient 46-S, before and after she received thyroid therapy.

a certain specificity or independence. This shows itself in discriminativeness in the responses to thyroid. Individual signs and symptoms recede at different times and rates. Figure 5 lists twenty-six clinical signs in the order of their disappearance in 46-S and 36-A and shows that order to be in general similar in the two cases. The vegetative or metabolic signs responded first, then the infiltrative, later the skeletal and lastly the psychoneurologic.

Figure 6 shows the same signs arranged in the order of their appearance in 36-A. The infiltrative signs are really terminal expressions of a condition of long standing, and they produce the classic features of cretinism listed below the middle line of the chart. A diagnosis of cretinism should, however, be made before the condition is full blown. An early diagnosis can be built up on the cumulative evidence of the thirteen items listed above the middle line. Each item in its turn and in its combinations strengthens the basis for at least a diagnostic test with thyroid.

Physical Growth—In both 46-S and 36-A the skeletal system was especially responsive to treatment. Roentgenograms taken before thyroid was administered (fig. 8) revealed marked retardation in the development of the carpal centers of both infants; 46-S at 46 weeks had one small carpal center instead of two,

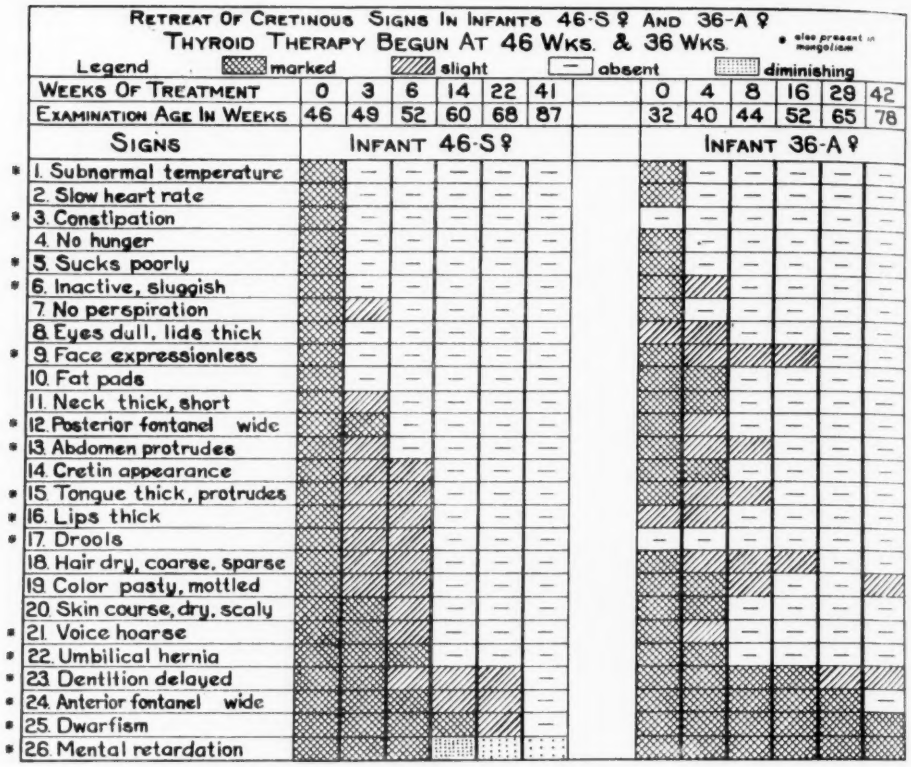
RETREAT OF CRETINOUS SIGNS IN INFANTS 46-S ♀ AND 36-A ♀
THYROID THERAPY BEGUN AT 46 WKS. & 36 WKS.
* also present in mongolism
Legend marked slight — absent diminishing
WEEKS OF TREATMENT 0 3 6 14 22 41 0 4 8 16 29 42
EXAMINATION AGE IN WEEKS 46 49 52 60 68 87 32 40 44 52 65 78
SIGNS INFANT 46-S ♀ INFANT 36-A ♀
* 1. Subnormal temperature
2. Slow heart rate
* 3. Constipation
4. No hunger
* 5. Sucks poorly
* 6. Inactive, sluggish
7. No perspiration
8. Eyes dull, lids thick
* 9. Face expressionless
10. Fat pads
11. Neck thick, short
* 12. Posterior fontanel wide
* 13. Abdomen protrudes
14. Cretin appearance
* 15. Tongue thick, protrudes
* 16. Lips thick
* 17. Drools
18. Hair dry, coarse, sparse
19. Color pasty, mottled
20. Skin course, dry, scaly
* 21. Voice hoarse
* 22. Umbilical hernia
* 23. Dentition delayed
* 24. Anterior fontanel wide
* 25. Dwarfism
* 26. Mental retardation

Fig. 5.—Chart showing the order of retreat of cretinous signs in 46-S and 36-A.

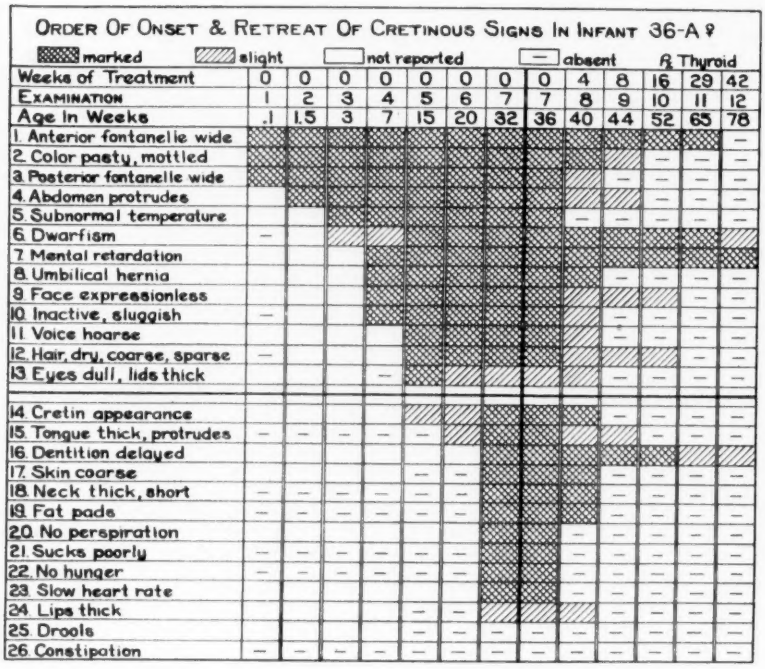
ORDER OF ONSET & RETREAT OF CRETINOUS SIGNS IN INFANT 36-A ♀
marked slight not reported — absent & Thyroid
Weeks of Treatment 0 0 0 0 0 0 0 0 4 8 16 29 42
EXAMINATION 1 2 3 4 5 6 7 7 8 9 10 11 12
Age in Weeks .1 1.5 3 7 15 20 32 36 40 44 52 65 78
1. Anterior fontanelle wide
2. Color pasty, mottled
3. Posterior fontanelle wide
4. Abdomen protrudes
5. Subnormal temperature
6. Dwarfism
7. Mental retardation
8. Umbilical hernia
9. Face expressionless
10. Inactive, sluggish
11. Voice hoarse
12. Hair, dry, coarse, sparse
13. Eyes dull, lids thick
14. Cretin appearance
15. Tongue thick, protrudes
16. Dentition delayed
17. Skin coarse
18. Neck thick, short
19. Fat pads
20. No perspiration
21. Sucks poorly
22. No hunger
23. Slow heart rate
24. Lips thick
25. Drools
26. Constipation

Fig. 6.—Chart showing the order of onset and retreat of cretinous signs in 36-A.

while 36-A at 14 weeks had none and lacked the center of the proximal epiphysis of the tibia, which is normally present at birth. After approximately a year of treatment 36-A showed normal carpal development, and 46-S, advanced carpal development, for their respective ages.

Other interesting changes in physical growth are brought out in figures 9 and 10, in which the measurements of 46-S and 36-A are shown side by side and compared with the anthropometric norms of Englebach.[3] Six physical measurements are plotted: weight, height, upper measure (from vertex to symphysis), lower measure (from symphysis to soles) and the circumference of the head and of the chest.

Patient 46-S, born of tall parents, was overweight at birth but showed dwarfing as early as the age of 14 weeks. By the time she was 46 weeks old all her measurements showed marked retardation in physical growth, the length of the

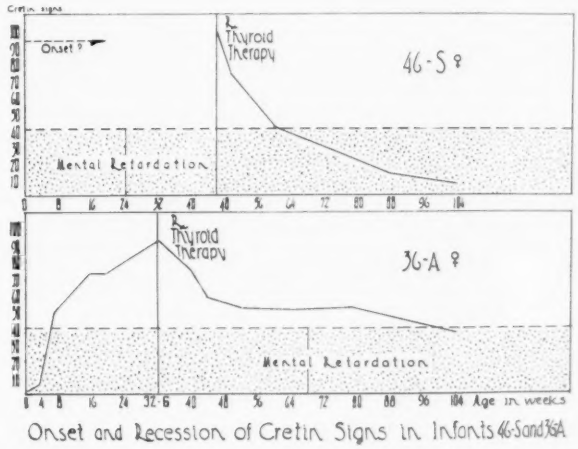

Fig. 7.—Curves illustrating the onset and recession of cretinous signs in 46-S and 36-A.

legs (lower measure) being excessively and disproportionately short. Immediately after treatment was instituted the weight and the circumference of the chest diminished, though the infant was taking food better than ever before; this was due to the loss of myxedematous and fatty infiltrations. A positive acceleration of increase in all the physical dimensions followed. The lag in the growth of the legs was strikingly overcorrected; the length of the legs reached the normative level in twenty-two weeks, whereas the trunk (upper measure) did not approach the normative level until nineteen weeks later, or after forty-one weeks of treatment. When the child was 2 years of age, after fifty-nine weeks of treatment, the circumference of the head and that of the chest were disproportionately large; the weight exceeded the maximal figure for her age, while the height measurements were all within the normal range.

3. Englebach, William: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 1, pp. 261-312.

Patient 36-A, at birth underweight but of normal height, was dwarfed by the time she was 15 weeks old. Loss of weight occurred at that time, associated with otitis media accompanied by parenteral diarrhea. As with 46-S, progressive, generalized physical retardation occurred before treatment, with a disproportionate lag in the growth of the legs. Loss of weight and diminution in the circumference of the chest took place at the onset of treatment and a positive acceleration in growth, with overcorrection of the length of the legs, followed.

The charts show the generalized though somewhat uneven effect of thyroid on the total complex of physical growth. In 36-A the complex remained consistently subnormal. At 2 years of age she was still dwarfed, but she was a long-legged dwarf, whereas before she had been a short-legged dwarf. Clearly, thyroid therapy has a specific influence on the length of the legs. Physical measurements of the other cretins in our series bear out this suggestion. For normal infants, similarly, the percentage of increase in the length of the legs in the first

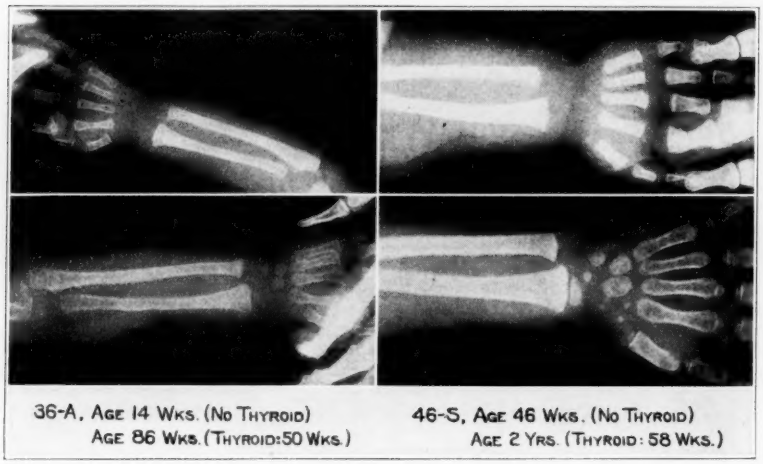

Fig. 8.—Roentgenograms showing the development of carpal centers in 36-A and 46-S.

year of life is greater than that in the length of the body as a whole (45 per cent versus 26.5 per cent, according to the Yale normative data on changes in body proportions).[4] The effect of thyroid therapy on cretinism may be visualized as a somewhat intemperate reenforcement of a potentially normal trend.

Mental Growth.—The importance of the skeletal and vegetative signs is clear. The indicators of the growth of the central nervous system are most in danger of being overlooked. What are these psychoneurologic indicators? They are the reaction patterns of the infant in the fields of posture, locomotion, prehension, language and adaptive and social behavior, and their maturity values may be expressed in terms of developmental quotient.

The course of mental growth of these two infants showed differences as profound as those in the physical field. In the case of 36-A we had fortunately

4. Gesell, A., and Thompson, H.: The Analysis of Behavior Growth, Including a System of Norms of Infant Development, to be published.

made three developmental examinations prior to diagnosis and treatment. The graph of mental growth (fig. 11) shows that the behavior levels when the child was 14, 20 and 32 weeks of age were definitely subnormal. It also shows a tendency of the severity of retardation to increase as cretinism developed. A slight amelioration followed prolonged treatment. The broken line we believe

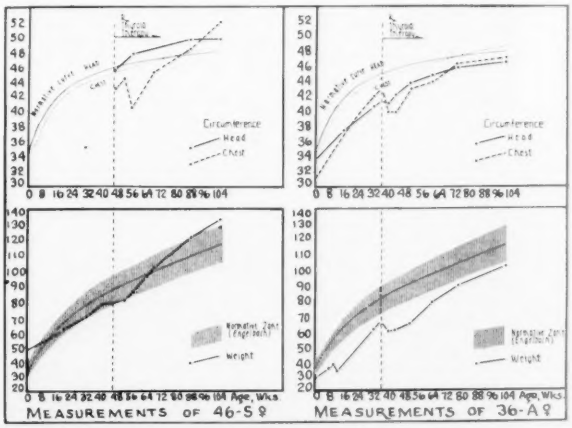

Fig. 9.—Curves showing a comparison of the circumference of the head, the circumference of the chest and the weight of 46-S and 36-A with the anthropometric norms of Englebach.

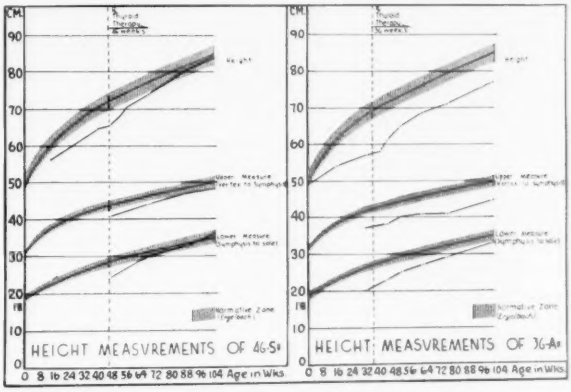

Fig. 10.—Curves showing a comparison of the height measurements of 46-S and 36-A with the anthropometric norms of Englebach.

to be a true prediction of the course of mental growth without thyroid therapy. When the child was 2 years of age her behavior was at a 14 month level; her developmental quotient had risen from 40 to approximately 60. The developmental quotient at the age of 2½ years (examination not charted) was identical with that at 2 years, and no further improvement occurred. Acceleration ceased, and the developmental ratio became relatively fixed at a defective level.

In the case of 46-S the influence of thyroid therapy on mental growth was consistent and unequivocal (fig. 12). Acceleration of mental development was prompt, and improvement was progressive. The developmental quotient rose from 50 to 90, and the child's mental status steadily advanced, from a defective level to a borderline level and then, at the age of 2 years, reached a definitely normal level. Reexamination at the age of 3 years (not charted) showed stabilization of the

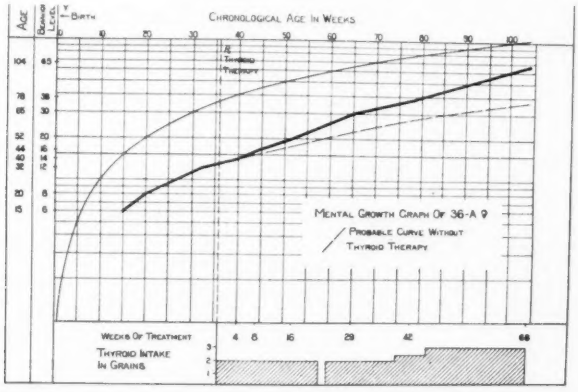

Fig. 11.—Curves showing the course of mental growth of 36-A.

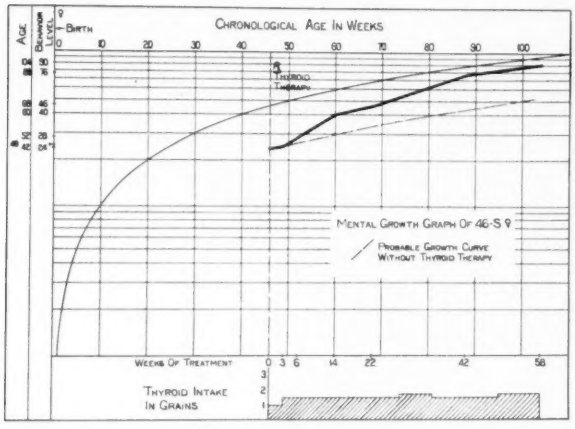

Figure. 12.—Curves showing the course of mental growth of 46-S.

developmental ratio at the normal level. The outlook with respect to mental status at the time of writing is entirely favorable.

Dynamic Characteristics of Behavior.—Cretinism does not necessarily produce a marked distortion or skewing of the normal patterns of behavior, but the tempo and perhaps the intensity of activity are seriously affected. In order to investigate the more strictly dynamic changes produced by thyroid therapy we subjected some of our cinema records to minute analysis. It may be briefly explained that the cinema films recorded the behavior displayed during the develop-

mental behavior examinations. These examinations[5] were made with standardized procedures under uniform conditions, with the child lying or seated in a specially designed crib, as pictured in figure 13. The camera recorded the behavior at an established speed of sixteen frames per second; there were forty frames per foot. The film was examined frame by frame with the aid of an analytic projection desk. Frames were counted to determine the time values, which were later plotted. In this way the responses of one child could be readily compared with those of another, and the film became a timing device, from which the rate of activity and the time required for a given performance could be computed.

Patients 46-S, who responded well to treatment, and 36-A, who responded poorly, were compared with O-N, a normal infant.[6] The child O-N was one of a group of normal children who had been intensively studied from the age of 4 weeks to 5 years. She was neither overactive nor lethargic in her behavior, and her development was representative of a normal, average course of physical and mental growth.

The prehensory, perceptual and manipulatory reactions of the infants to such objects as single and multiple cubes, a pellet, a bell, a ring and string were analyzed. The cretin subjects were studied before and after thyroid therapy,

Fig. 13.—Patient 46-S in the behavior examination crib.

while the normal subject was studied at selected ages, giving us both the mental and the chronological age equivalents for comparison. Thus, 46-S at 46 weeks was matched with O-N at 24 and at 44 weeks, while at 60 weeks she was matched with O-N at 40 and at 60 weeks. In each case from six to ten behavior situations, yielding from forty to sixty minutes of performance, were analyzed at each age level, and the following dynamic behavior characteristics were quantitatively determined: (1) number of shifts of regard per minute; (2) number of movements of the head per minute; (3) number of movements of the more active arm per minute; (4) number of movements of both arms per minute; (5) number of seconds of delay after the presentation of an object before the prehensory approach, and (6) duration of approach, in seconds. (For 36-A at 34 weeks and O-N at 12 weeks, items 5 and 6 were omitted, since true prehensory approach was absent.)

5. Gesell, A.; Thompson, H., and Amatruda, C. S.: Infant Behavior: Its Genesis and Growth, New York, McGraw-Hill Book Company, 1934, p. 343.

6. The behavior patterns of this infant, as G 48, are delineated in detail in Gesell, Arnold: An Atlas of Infant Behavior: A Systematic Delineation of the Forms and Early Growth of Human Behavior Patterns. I. Normative Series, in collaboration with Helen Thompson and Catherine Strunk Amatruda, New Haven, Conn., Yale University Press, 1934.

The six graphs in figure 14 summarize the results in the case of 46-S. The solid lines show the trends for the normative infant, O-N. The broken lines show the trends for 46-S; the dotted line is drawn with the developmental levels of 46-S and O-N equated and the dash line with the chronological ages equated. The graphs clearly show that the rate of activity of 46-S was subnormal both for the age range and for the developmental range plotted. In each instance, however, the rate of activity increased faster than is normal for that range. Cinema analysis of 36-A's behavior yielded similar results (fig. 15).

This dynamic improvement is an interesting phenomenon, based on metabolic or energy utilization factors controlled by thyroxine. A distinction must be made between the immediate physiologic effects of thyroxine on the dynamics of behavior

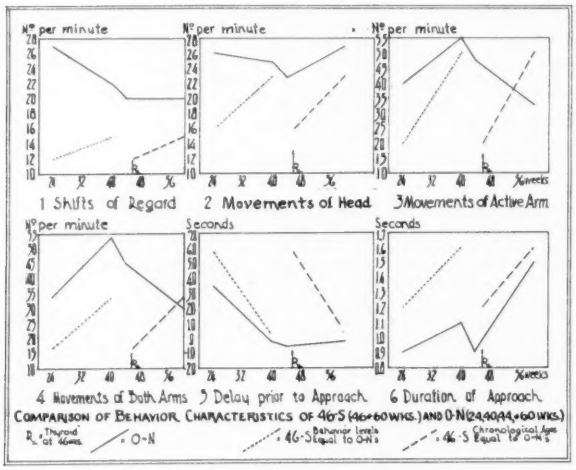
No per minute
No per minute
No per minute
1 Shifts of Regard
2 Movements of Head
3 Movements of Active Arm
No per minute
Seconds
Seconds
4 Movements of Both Arms
5 Delay prior to Approach
6 Duration of Approach
COMPARISON OF BEHAVIOR CHARACTERISTICS OF 46-S (46+60 WKS.) AND O-N (24-44+60 WKS.)
R = Thyroid at 46 mos.
= O-N
= 46-S Equal to O-N's Behavior Levels
= 46-S Equal to O-N's Chronological Age

Fig. 14.—Six graphs showing a comparison of the behavior characteristics of 46-S with those of a normal infant (O-N).

and the long range effects on the neurologic growth cycle, or the morphogenesis of the maturing patterns of behavior. It is significant that in 36-A considerable dynamic improvement was associated with meager developmental progress.

COMPARISON OF 105-L AND 27-M

The two children 105-L and 27-M are of interest because their development under thyroid therapy was followed for a prolonged period. Both children were unmistakable cretins in infancy. One received treatment for six and one-half years and the other for more than nine years. Each became normal in physical appearance (fig. 16). In both the skeletal response to treatment was apparently complete. Roentgenograms of 105-L at the age of 2 years indicated retardation in the development of the carpal and tarsal bones. At the age of 9 years the calcaneus was normally developed. Figure 17 shows early roentgenograms of 27-M. At the age of 6 months she had no carpal centers, and at 15 months, after nine months of thyroid therapy, she showed four carpal centers, a spurt to the 4 year (carpal) level, and the elbow presented a center for the capitellum.

which normally appears at the age of 17 months. Finally, both children achieved normal stature. At this point the similarity between them ceased.

Of the two, 27-M was originally more retarded, but she was less dwarfed and her treatment was begun earlier. Figure 18 summarizes the early course (from the age of 6 to 33 months) of physical and mental growth under thyroid therapy. The height became normal within the first thirteen weeks of treatment, and the developmental rate accelerated markedly within four weeks. Steady improvement continued, and in somewhat less than a year a modest, but normal, degree of intelligence was attained. The mental status underwent consistent growth, thanks to thyroid. The child consumed over 1½ troy pounds (560 Gm.) of thyroxin in ten years. In figure 19 are plotted the twenty-six successive measurements made

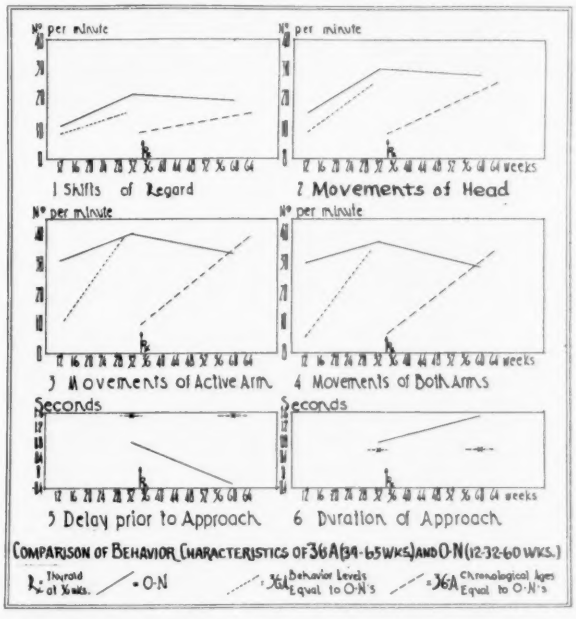
N° per minute
1 Shifts of Regard
2 Movements of Head
3 Movements of Active Arm
4 Movements of Both Arms
Seconds
5 Delay prior to Approach
6 Duration of Approach
weeks
COMPARISON OF BEHAVIOR CHARACTERISTICS OF 36A (34-65 WKS.) AND O-N (12-32-60 WKS.)
Thyroid at 36 wks.
O-N
36A Behavior Levels Equal to O-N's
36A Chronological Ages Equal to O-N's

Fig. 15.—Six graphs showing a comparison of the behavior characteristics of 36-A with those of a normal infant (O-N).

during the ten years of observation. The mental quotient remained in or near the 75-85 zone. Irregularities of intake declared themselves in irritability, constipation, diarrhea and even convulsions at various times, as indicated in the chart. At the age of 9 years temporary myxedema developed, owing to a pharmaceutic error. The druggist performed the experiment! For one month the child was fed thymus instead of thyroid. Cretinous signs at once emerged, but retreated when thyroid was restored. This child's normality surely hung on a thyroid thread.

Patient 105-L had the disadvantage of starting treatment at the relatively late age of 2 years. Although she was slightly less retarded when she was first examined than 27-M, she had nevertheless a serious grade of mental defect, and dwarfing was more marked. Her response to treatment showed a very

different picture (fig. 20). After six months of treatment physical growth began to accelerate, but not until a year had elapsed did the height even approach the normal. The developmental response in behavior abilities was even more sluggish, and the first appreciable gain did not occur for eighteen months. During the succeeding years no further rise in developmental quotient occurred. At

Fig. 16.—*A*, 105-L at the age of 9 years. *B*, 27-M at the age of 10 years.

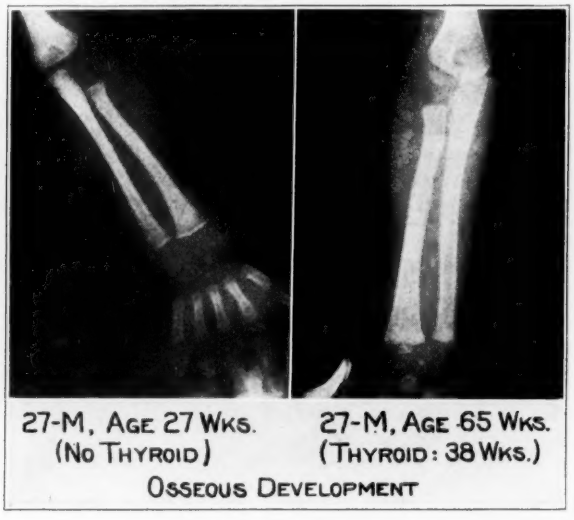

Fig. 17.—Roentgenograms of 27-M, showing the development of carpal centers.

8½ years of age 105-L had a mental age of 3⅓ years (developmental quotient, 40), and institutional care was advised, while 27-M at the same age was in the second grade at school.

COMPARISON OF 80-H AND 21-F

The history and clinical course of 80-H and 21-F are outlined in table 1. These patients did not differ significantly from those already described as responding favorably to thyroid treatment. Patient 21-F was of particular interest to us

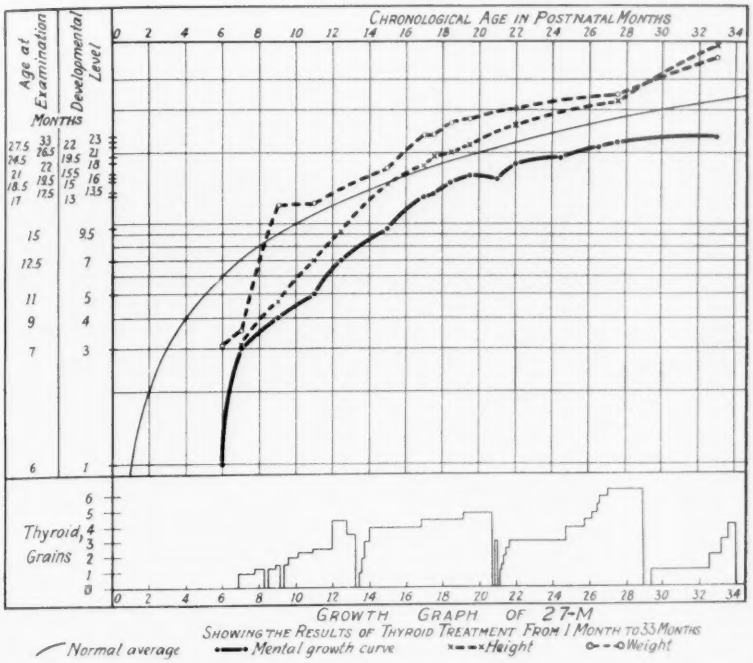

Fig. 18.—Curves showing the early course of physical and mental growth of 27-M under thyroid therapy.

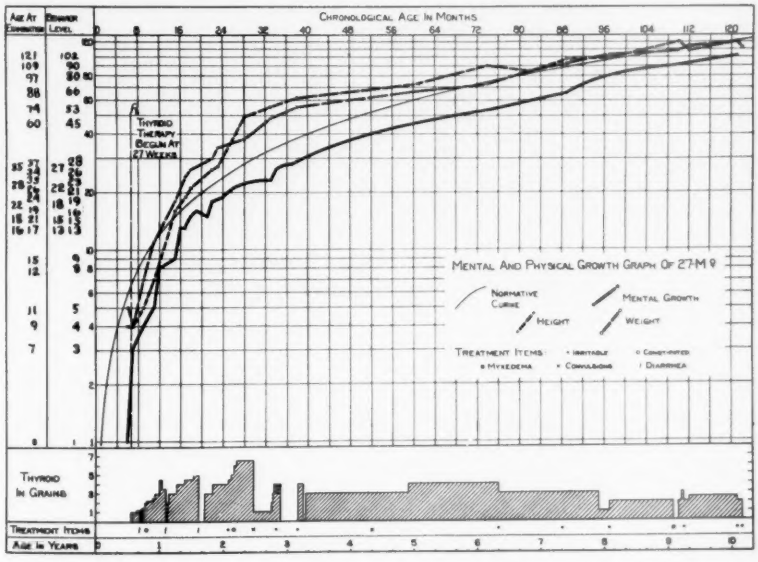

Fig. 19.—Curves showing the physical and mental growth of 27-M during ten years of treatment.

because we made a prognostic error in her case. She presented a congenital malformation of the left nostril, a coloboma of the choroid and iris of the left eye and a corneal dermoid cyst. Her appearance was decidedly stigmatic. In her early infancy we concluded, too readily, that the physical abnormalities denoted a deep-seated and pervasive developmental defect and that the hypothyroidism was, in Tredgold's sense, "a superadded complication." The event proved that we were mistaken. The child's mental improvement surpassed expectations. Although set in an environment of developmental anomalies dating back to the early embryonic period, the neuro-endocrine system was not radically impaired and responded sufficiently to take this infant at least out of the definitely defective group. She illustrates strikingly the specificity of developmental assets and

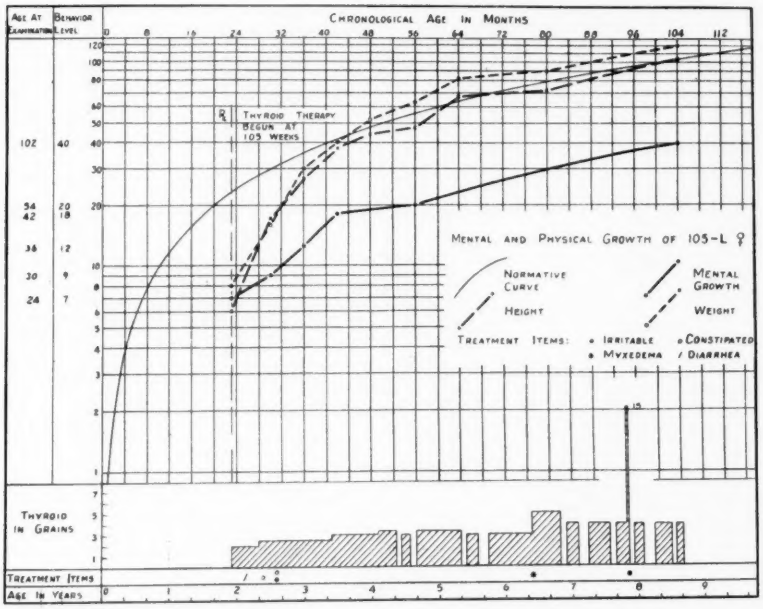

Fig. 20.—Curves showing the physical and mental growth of 105-L during six and one-half years of treatment.

liabilities and of the associated factors of "insurance" and regulation. Thyroid therapy helps to define the strength of those factors, which, of course, are fundamentally chemical.

PROGNOSIS CRITERIA

Of our group of children, two remained defective under treatment, while four attained at least a fair degree of normality. Are there any prognostic criteria which distinguish cretins who are potentially normal from cretins who are refractory to treatment?

In general appearance all the infants in our group showed the classic signs of full-blown cretinism when treatment was begun. In one infant a single item may have been absent or less pronounced than in another, but no significant variations or trends were observed.

All the treated patients lost the cretin facies and habitus, even those in whom serious mental deficiency persisted. In the field of personality, although emotional responses became more vivid, the "normal" children continued to show a certain docility and placidity typical of the cretin constitution. The defective children, as they grew older, showed in addition a tendency to deterioration of behavior response in any given situation; for example, in a simple form board test, of three trials the first reaction was, typically, the best and the third the poorest. This seemed to be due to a peculiar kind of fatigability based on specific biochemical limitations.

The prognostic significance of the optimal therapeutic dosage deserves more study. Six cases do not permit general conclusions. However, it appears that infants who react favorably to treatment respond best to comparatively small doses of the dried gland and are intolerant of larger doses. The patients who reacted unfavorably did not show this intolerance but were only slightly benefited by larger doses.

TABLE 2.—*Change in the Developmental Quotient and the Height Index Under Treatment* *

Patient	105-L	36-A	80-H	21-F	46-S	27-M
Mental status attained	D	D	N	N	N	N
Age at which thyroid therapy was begun	105 wk.	36 wk.	80 wk.	21 wk.	46 wk.	27 wk.
Original developmental quotient	25	40	50	45	50	15
Gain in developmental quotient	15	20	25	30	40	65
Developmental quotient attained	40	60	75	75	90	80
Original height index	25	25	27	45	50	65
Height index attained	100	60	128	85	97	100

* D indicates defective; N, normal.

Table 2 summarizes the main factors which must be considered in a discussion of prognostic criteria.

The age at which treatment is begun and the severity of the retardation at that time are generally considered important. In our cases we were unable to establish a close correlation between the developmental response and the age factor. Our experience with 36-A proves that early treatment is not always effective and with 80-H, conversely, that delayed treatment, at least up to a certain point, does not necessarily preclude a favorable response. Nor can the outcome be directly related to the severity of the original retardation, since 27-M, the infant with the most marked retardation (developmental quotient, 15) made the remarkable gain of 65 points and at the age of 10 years was classifiable as normal.

It is of course possible that the improvement in 80-H might have been more striking if therapy had been instituted earlier. To support this contention it can be pointed out that her gain in developmental quotient was only 25 points. This is below the average increment for

the group (33 points) and is smaller than the increase for any of the other patients whose response to treatment was favorable. Nevertheless, this gain brought 80-H into the normal fold, and her therapeutic response has to be classed as good even if we grant that it might have been better.

Before our acquaintance with 80-H we might have considered the amount of dwarfing of real significance. Dwarfing is expressed in terms of the height index, the ratio between height age and chronological age, in accordance with the Engelbach norms. A height index of 50, for example, does not mean that the child is half the normal height; it means that his height equals that of a child half his age. Patients 36-A and 105-L, the two who remained defective, each had a height index of 25 before treatment; while all the children whose treatment had favorable results, with the exception of 80-H, had an index of 45 or more. Patient 80-H, however, had an original height index of only 27, and her course shows that the original degree of dwarfing is without consistent prognostic import.

TABLE 3.—*Influence of Thyroid Therapy on the Height Index* *

Patient	Mental Status	Duration of Therapy	Original Height Index	Height Index Attained	Height Index After 6 Mos. of Therapy
105-L	D	7 yr.	25	100	57
36-A	D	21 mo.	25	60	51
80-H	N	18 mo.	27	128	77
21-F	N	14 mo.	45	85	75
46-S	N	26 mo.	50	97	82
27-M	N	10 yr.	65	100	80

* D indicates defective; N, normal.

These considerations only emphasize how innate, and therefore individual, the response to treatment is and how little the response, apparently, is affected by what might seem to be important determiners. The difference between the patients who reacted favorably to treatment and those who did not is reduced to a difference in response to treatment. The patients who eventually attained a normal outlook showed a prompt acceleration in both mental and physical development. The take-up or immediacy of therapeutic response is therefore an important prognostic indicator.

No matter how low the original height index was for the patients for whom treatment was effective, the acceleration of growth took place promptly and, the height index reached 70 or above within six months of the initiation of treatment. The case of 105-L, who attained normal stature though she remained mentally defective, illustrates the reverse of this fact. A year of treatment was required to bring her height index to 70. For 36-A the height index was only 60 after twenty-one months of treatment. These relationships are summarized in table 3.

In the field of behavior, also, the readiness of therapeutic response gives the prognostic clue. A gain of 10 points or more in the developmental quotient was considered significant. The time required for the first real gain to appear bears an inverse relationship to the total gain. The last two columns in table 4 show that a quick initial gain

TABLE 4.—*Influence of Thyroid Therapy on the Mental Status* *

Patient	Mental Status	Original Developmental Quotient	Developmental Quotient Attained	No. of Months Therapy Before Total Gain in Developmental Quotient	Total Gain in Developmental Quotient	Duration of Therapy Before Initial Gain of 10 Points in Developmental Quotient, Weeks
105-L	D	25	40	18	15	78
36-A	D	40	60	15	20	68
80-H	N	50	75	18	25	36
21-F	N	45	75	14	30	31
46-S	N	50	90	13	40	14
27-M	N	15	80	12	65	4

* D indicates defective; N, normal.

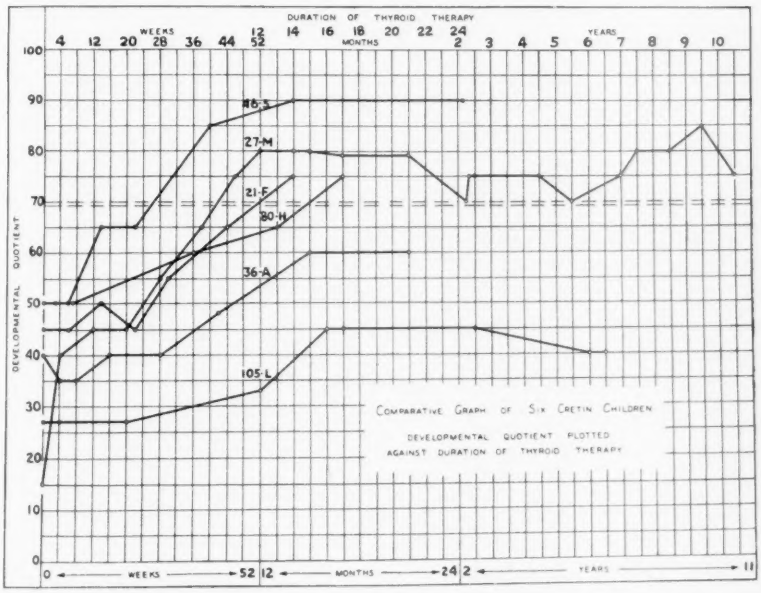

Fig. 21.—Curves showing the changes in the developmental quotient of the six children. The broken line indicates the approximate low limit of normal intelligence.

augured a large total gain; the more delayed the initial gain, the smaller the total increment. If the response was delayed over a year the total increment was so small that the child remained defective.

When all the cases are reviewed, it is evident that the first two years of treatment are of critical importance (table 4 and fig. 21). Indeed,

the entire gain in the developmental quotient was accomplished in that period.

The indications also are that the maximum quotient, once achieved, is maintained indefinitely as long as feeding with thyroid is continued.

GENERAL CONCLUSIONS

The effects of thyroid substance on the cretinous infant are of three kinds: (*a*) metabolic, or dynamic, (*b*) somatic and (*c*) neurodevelopmental.

The metabolic effects, which involve the vegetative system and the dynamics of behavior, are the most immediate and general.

Marked physical improvement occurred in all our cases, with development of a normal appearance and acceleration in physical growth, particularly in the length of the legs.

The mental status under treatment varied widely, from persisting severe mental deficiency to normal intelligence.

Every cretin has a latent and distinctive optimal response, which is probably favored by early treatment.

The ultimate response can be forecast by repeated careful determinations of physical growth and of behavior status during the early months of treatment.

The therapeutic effects of thyroid substance depend on factors of biochemical readiness in the organism. It is a reasonable assumption that the primary effect is on the thyroid itself and on associated glands, enabling them to resume their regulatory functions. The final influence on the cretin is therefore contingent not so much on the age of the child or his maturity status at the time of diagnosis as on the residual physiologic capacity and the latent growth potency of his neuro-endocrine system. Thyroid therapy cannot bring about normality if there has been a fundamental impairment of that system, hereditary or developmental. The initial response to treatment is part of a total symptomatology, and at the same time it is an index of the reserve capacity of the neuro-endocrine system. This response cannot be fully determined without a diagnosis of the behavior status. The development of the central nervous system can be tested only by an appraisal of the infant's behavior patterns. Such an appraisal of behavior maturity is part of the task of the clinical pediatrician and is essential to a timely diagnosis and prognosis of cretinism in infancy.

Case Reports

IDIOPATHIC HEMORRHAGIC SARCOMA (KAPOSI)

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NEW YORK
AND
HOWARD C. LEOPOLD, M.D.
PHILADELPHIA

Multiple idiopathic hemorrhagic sarcoma, an unusual disease among adults in America, is rare in children. Our case is particularly interesting because the condition was typical both clinically and pathologically.

REPORT OF A CASE

The patient was a 4½ year old boy, American born of Italian parents. He was one of unidentical twins. The parents and ten siblings were living and well. The previous history was irrelevant.

One year prior to admission of the patient to the hospital two "blue spots," attributed by the family to trauma, were noted on the left leg. Two months before he entered the hospital firm, painless "lumps" were observed in both groins. Recently several new lesions were seen on the trunk, and blood specks were noted in the stool.

Examination showed positive findings only in the skin and the lungs. There were two lesions, each about 2 cm. in diameter, in the middle third of the left leg; they were purplish, raised, painless nodules, one of which was soft and almost fluctuating. Below the internal malleolus of the right ankle and the external malleolus of the left and at the base of two toes there were dark, firm, purplish red plaques. In addition, scattered over the lower part of the abdomen were several greenish, infiltrated lesions, painless and attached to the skin. The cervical, axillary and inguinal glands were palpable, and two large, hard nodes were found in the right inguinal region. Coarse râles and slightly impaired resonance were noted at the base of each lung. The spleen was not palpable. The tonsils were enlarged; no lesions were seen in the nose, pharynx or larynx. Digital rectal examination gave negative results, and because of a history of blood in the feces a sigmoidoscopy was done. This also gave negative results. Roentgen examination of the skull and the long bones showed no abnormality.

The findings with regard to the blood were within normal limits, and over a period of months there was little change.

On the child's admission to the hospital the question arose as to whether he was suffering from purpura and a blood dyscrasia or from a neoplastic disease.

From the Pediatric Service, Mount Sinai Hospital, New York, Dr. Béla Schick, director.

A complete bibliography is to be found in the papers of Kren and Dörffel.

The relative chronicity of the lesions, their induration and the negative blood picture pointed to the probable existence of a neoplastic condition, and further study and biopsy confirmed this impression.

All other laboratory data were essentially negative and are recorded here only for completeness. The blood chemistry and the results of dextrose tolerance tests were normal. The urine showed a trace of albumin, a rare white blood cell and urobilin in a dilution of 1 : 20. The heterophile reaction was moderately positive. Blood culture showed no growth, and agglutination tests for typhoid and paratyphoid bacilli were negative. Tuberculin tests also were negative.

One of the hemorrhagic nodules on the left leg was removed. The report on it was "papillary angiomatous tumor with spindle cells," characteristic of Kaposi's hemorrhagic sarcoma. The pathologic aspect will be discussed later.

Fig. 1.—Note the indentation or puckering of the lesion just above the enlarged inguinal gland. This indicates involution or fibrosis of the central part of the lesion while extension continues at the periphery. Just below the inguinal region is the fibrous type of lesion passing inward along the femoral vessels.

The course of the disease was at first stationary and thereafter slowly and progressively downward during the four and one-half months that the patient has been under observation in the hospital. The status at the last examination prior to the writing of this report will be described, with reference to earlier lesions to indicate the nature of their evolution. There were bluish discolorations on the bridge of the nose, hair line and right eyebrow, and there was a mass about 1 inch (2.5 cm.) long in either the periosteum or the bone of the right frontal region.

The left lower quadrant of the abdomen was filled with oblong infiltrated masses involving the skin and deeper structures and extending horizontally toward the right side. In places these oblong masses were yellowish and blue. Similar

indurated, purplish lesions were present near the umbilicus and the left costal margin. The large nodule in the right inguinal region showed peeling following radiotherapy.

The arms showed only two small purplish nodules.

The lesions on the back revealed the tendency to follow the course of the blood vessels even more characteristically than did those of the legs or of the abdomen. From the lower dorsal region to the sacrum there were rows of oblong greenish blue, indurated masses extending laterally from the spine like the rungs of a ladder, obviously following the course of the lumbar and lower intercostal vessels.

Fig. 2.—Condition of the left leg.

The legs in particular demonstrated the vascular and fibrotic elements and their varying predominance in the evolution of the lesions. When the child was admitted to the hospital there were fairly firm cords running from the groin inward, puckering the skin and following the femoral vessels. On the surface were a few yellowish and bluish discolorations. These were primarily fibrotic, and in the course of months they have become even firmer. At the last examination they could be traced down along the vessels to below the knee, and distally

individual nodules could be felt like beads on a string. The left leg was edematous, probably owing to the constriction of blood and lymph vessels by the fibrotic cords, which on this extremity extended laterally as well as mesially. At the knees contractures had developed, and the legs were held in partial flexion. On the lower part of the left leg were two purplish nodules from ½ to 1 inch (1.25

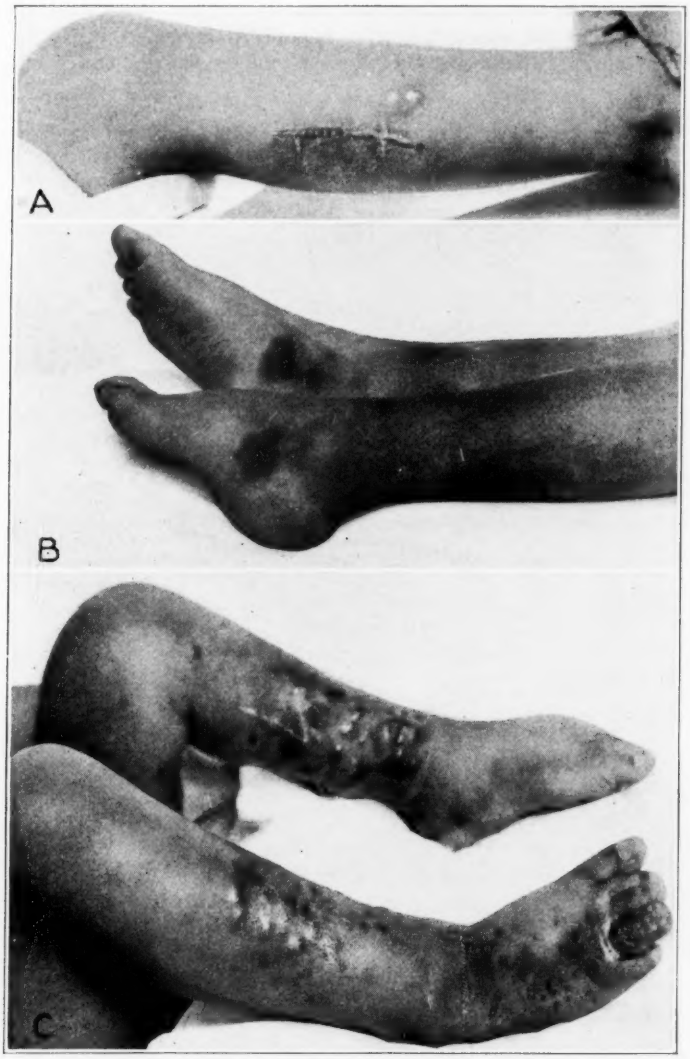

Fig. 3.—*A*, condition of the left leg of the child on his admission to the hospital. The biopsy specimen from the lower part of the wound resembled that pictured in figure 4. *B*, flat, firm, violaceous plaques representing probably the mixed fibrous and vascular type of lesion. *C*, the condition of the legs five months after admission of the child to the hospital. The flexion of the legs is due to contractures.

to 2.5 cm.). in diameter bulging above the surface. One of them even fluctuated. These represent the primarily vascular element of hemorrhagic sarcoma. Some of these purplish vascular nodules have increased in size and have maintained their soft fluctuating consistency. This indicates that not all lesions pass from a hemorrhagic to a fibrotic stage, but some remain essentially angiomatous through the whole course of the disease. Finally, about the malleoli and the bases of the toes there were flat, hard, reddish purple plaques, probably to be interpreted as admixtures of fibrotic and vascular elements. About one month prior to the writing of this report several dozen small purpuric lesions resembling petechiae appeared on the left thigh. These "petechiae" developed into typical purplish raised hemorrhagic nodules from a few millimeters to a centimeter or more in size. Many of them are soft and fluctuating, but others have become firm.

Râles heard at the bases of the lungs at the time that the child was admitted to the hospital soon disappeared. Impaired resonance persisted, and pulmonary infiltration was confirmed by roentgen examination. This infiltrative process has increased in extent and intensity. The negative results of tuberculin tests and the absence of fever warrant the assumption that this infiltration is of sarcomatous and not inflammatory origin.

The therapy has consisted in the use of roentgen rays, confined at first to the right inguinal region, which presented the largest swelling of the lymph glands. The treatment has been under the direction of the radiotherapy department, and the dose used was 200,000 kilovolts, filtered with 2 mm. copper and 1 mm. aluminum at a distance of 50 cm., from 100 to 200 roentgens being administered at each sitting. Twenty-four treatments were given during seven weeks. Treatment was discontinued because of failure to arrest the progress of the disease. Dermatologic consultants suggested the use of arsenic but without great enthusiasm or conviction concerning its efficacy.

The prognosis is bad. The progress of the disease has been more rapid in the four months of residence in the hospital than in the previous year following the onset of the disease. Unless spontaneous improvement occurs or some new and as yet unknown remedy is found, both very remote possibilities, one may anticipate steady but slow advance of the disease until intercurrent infection or hemorrhage from the lung or other vital organ causes death.

COMMENT

Kren [1] stated:

The cardinal changes that characterize Kaposi's sarcoma histologically consist of new growth and ectasia of capillaries, hemorrhage and proliferation of connective tissue. The vascular changes concern primarily the blood vessels and only to a lesser extent the lymph vascular system. Pigmentation develops from hemorrhage, and reaction processes occur about vascular and connective tissue, finally reaching the stage of involution and healing with lesions resembling scar tissue. Nevertheless, the histologic pictures are very different, depending on whether vascular or fibrous changes predominate in the tissue and whether circumscribed or diffuse cellular proliferation develops.

Although Kren devoted eighteen more pages to the detailed description of the histologic picture, this brief introduction presents the essential features.

1. Kren, O., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3, pp. 891-1004.

The cutis is the site of development of the lesions. The epidermis is encroached on only secondarily by the advancing process. The first changes consist of capillary dilatation and capillary budding. The newly formed ectatic capillaries appear to be angiomas and have been described as such. Between the bundles of capillaries there are delicate, spindle-like fibroblasts. Depending on whether the vascular or the

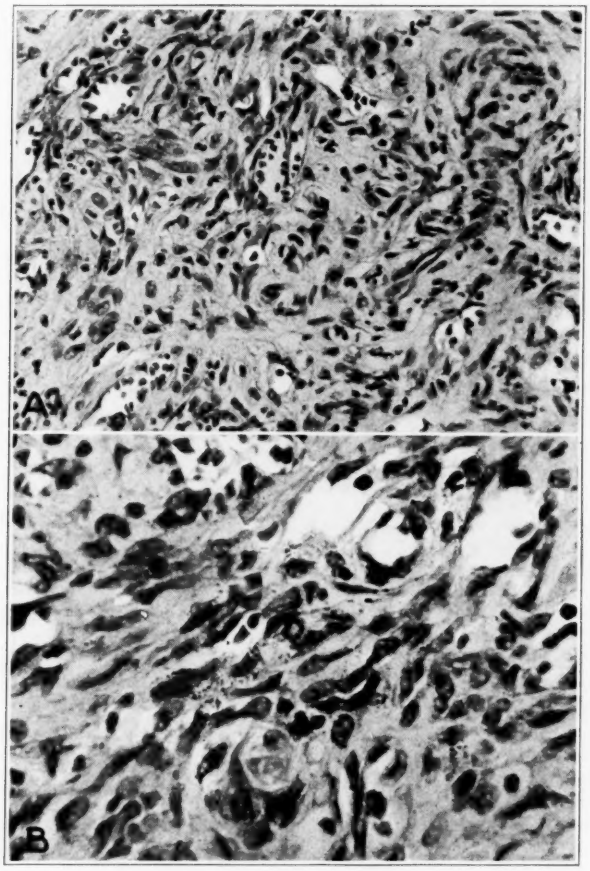

Fig. 4.—*A*, photomicrograph showing an area of the tumor composed of numerous dilated capillaries and intervening spindle cells (fibroblasts). *B*, high power photomicrograph showing the characteristic components, capillaries and spindle cells.

fibroblastic elements predominate, the lesion will be principally angiomatous or fibrous. In the gross description of the cutaneous lesions of our case, the varying rôles of vascular and fibrous tissue were emphasized. Some of the lesions from their inception seemed to be predominantly vascular and others predominantly fibrous, though neither

group was entirely one or the other. The fibrous lesions either retained their original characteristics or became more firm and fibrotic, causing the skin to pucker and contract, and the fibrous masses advanced inward between the muscles. Involution occurred in the center of lesions, even while at the periphery the process advanced. Some of the vascular tumors maintained their original character as soft, purplish masses; others became fibrous and developed as did the fibrous lesions.

The disease is rare in America and among Americans. It is found chiefly in urban centers where there is a heavy admixture of foreign population. The distribution seems to be geographic rather than racial; most of the cases come from Russia, Poland and Italy.

In childhood, the disease is particularly uncommon. In Dörffel's series of 365 cases the ages of 219 of the patients were mentioned.[2] The disease occurred in the first decade in fewer than 1 per cent of these. Several cases reported as having occurred in children were excluded by Kren. He expressed the belief that, in addition to manifestation of the typical course of the disease, the characteristic histologic picture should be shown in biopsy or autopsy specimens. According to these rather exacting criteria, Kren excluded McLean's case,[3] in which neither biopsy nor autopsy had been done. For similar reasons he eliminated the cases of Koebuer, De Amicis, Ochs and Billroth. We are not equipped to pass judgment on the minimal criteria for the diagnosis of Kaposi's disease, nor is it important that we should do so; rather we are calling attention to the question to emphasize the rarity of the disease in childhood.

Nearly every organ of the body may be subject to the disease. Thus, typical lesions have been recorded in the trachea, the laryngeal cartilages, the lungs, the bronchi and the pleura; in every part of the digestive apparatus from the esophagus to the anus; in the liver, the spleen, the kidneys, the adrenals and the bladder, and in all the lymph glands, superficial and deep. Among the endocrine glands, the testes, hypophysis and pancreas have been reported as harboring the nodules. The heart and pericardium are attacked rarely; on the contrary, the peripheral veins, arteries and lymph vessels are usually affected. All parts of the bones may be involved—epiphysis, diaphysis, marrow and periosteum. Lesions in the muscles, though rare, have been reported, particularly in the diaphragm and the intercostal muscles. No lesions have been found in the substance of the brain or cord, but the dura supposedly has been involved in one case.

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2. Dörffel, J.: Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, Arch. Dermat. & Syph. **26**:608 (Oct.) 1932.

3. McLean, S.: A Case of Idiopathic Hemorrhagic Sarcoma of Kaposi, Am. J. Dis. Child. **21**:437 (May) 1921.

From a recitation of the widespread distribution of the lesions one would be led to think of the extracutaneous lesions as metastatic. Students of the disease believe that the visceral lesions are not metastatic but primary foci, developing independently in each of the organs.

Origin of the cells in Kaposi's sarcoma and the pathogenesis and classification of the disease have been subjects of dispute. The degree of uncertainty surrounding these questions and the difficulty which dermatologists meet in arriving at a definite opinion are reflected in the comment of MacKee and Cipollaro,[4] which we quote:

> It is our belief in the light of present knowledge, that Kaposi's sarcoma is caused by an unknown systemic agent that attacks the vascular apparatus, causing chronic hyperplastic inflammation and granulomas and that the histogenesis is compatible with and undistinguishable from that of a malignant new growth or neoplasm. Ewing, Dillard and Weidman, Dörffel and, in fact, most authors agree that true sarcoma is produced; a number of authors do not think so. Frankly, we do not know, but we prefer to accept sarcoma until it has been definitely refuted.

From the point of view of the pediatrician the important diagnostic problem in cases of Kaposi's sarcoma is to avoid mistaking it for purpura and a blood dyscrasia. Then the exact diagnosis must depend on the report of a biopsy. The evolution and chronicity of the disease favor neoplasm rather than blood dyscrasia. However, a normal blood count does not exclude the possibility of leukemia; repeatedly, almost up to death, examinations of the blood of a patient with leukemia have given essentially normal results, and in the early stages of the disease a normal count is not at all unusual. It is our impression that McLean's case might well have been an instance of leukemia in spite of a nonleukemic blood picture and that classification of the condition as sarcoma of Kaposi in the absence of biopsy is inadvisable, as Kren has stated.

The therapeutic problem belongs in the realm of radiotherapy and dermatology. Arsenic, roentgen rays and radium are the means usually employed to check the disease. It is MacKee's opinion that treatment is of little avail—"that, while the agent causes involution of the eruption to which it is applied . . . it does not prevent the development of new lesions in various parts of the body." This occurred in the patient whose care we are reporting; indeed, there was little involution even in the lesion exposed to treatment with roentgen rays.

Prognosis presents interesting contradictions. The disease is steadily progressive, but its advance is so slow that the patient may outlive what otherwise would be a fatal disease. The condition has been known to exist as long as forty years. On the other hand, it may

4. MacKee, G. M., and Cipollaro, A. C.: Am. J. Cancer **26**:1, 1936.

be fatal within eight months. Death is due as a rule either to intercurrent infection or to sarcomatous lesions in the vital organs, particularly the lungs and intestinal tract, causing fatal hemorrhage.

SUMMARY

A case of multiple idiopathic hemorrhagic sarcoma of Kaposi is described and discussed.

NOTE.—Since the writing of this paper, the patient whose case we reported has died. Autopsy confirmed the diagnosis and showed extensive lesions characteristic of idiopathic hemorrhagic sarcoma.

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OSTEOPETROSIS ("MARBLE BONES")

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In 1904 Albers-Schönberg [1] described a disease of the skeletal system which he called *Marmorknochenkrankheit*. In the thirty-two years which have elapsed since this contribution was made less than eighty additional cases have appeared in the literature, under such diverse names as osteopetrosis,[2] Albers-Schönberg's disease,[3] osteosclerosis fragilis generalisata,[4] marble bones,[5] chalky bones,[6] osteosclerotic anemia,[7] *maladie des os marmoréens* [8] and congenital osteosclerosis.[9]

The characteristic evidence of this disease is the roentgen demonstration of the overgrowth of the cortical portion of the bone at the expense of the medullary cavity. This condition is usually most noticeable in the central portions of the pelvic bones, the bodies of the vertebrae, the bones at the base of the skull, the upper end of the femur and the lower end of the tibia and the fibula.[10] Certain secondary manifestations usually, although not invariably, accompany the disease process. They include multiple fractures, chronic osteomyelitis, epiphysial deformity, physical underdevelopment, hydrocephalus, atrophy of the optic

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From the Children's Psychiatric Ward of the Bellevue Hospital.

Read before the New York Academy of Medicine, Section of Pediatrics, May 14, 1936.

1. Albers-Schönberg, H.: Röntgenbilder einer seltenen Knochenerkrankung, München. med. Wchnschr. **51**:365, 1904.

2. Karschner, R. G.: Osteopetrosis, Am. J. Roentgenol. **16**:405, 1926.

3. Clairmont, P., and Schinz, H. R.: Case of Albers-Schönberg's Marble Bones, Arch. f. klin. Chir. **132**:347, 1924.

4. Davis, G. B.: Osteosclerosis Fragilis Generalisata, Arch. Surg. **5**:449 (Nov.) 1922.

5. Alexander, W. G.: Report of a Case of So-Called "Marble Bones," Am. J. Roentgenol. **10**:280, 1923.

6. Pirie, A. H.: The Development of Marble Bones, Am. J. Roentgenol. **24**:147, 1930.

7. Robertson, G. E.: Congenital Osteosclerosis, J. Pediat. **3**:439, 1933.

8. Pehu, M.; Policard, A., and Dufourt, A.: L'ostéopétrose ou maladie des os marmoréens, Presse méd. **39**:999, 1931.

9. Ghormley, R. K.: A Case of Congenital Osteosclerosis, Bull. Johns Hopkins Hosp. **33**:444, 1927.

10. McCune, J. D., and Bradley, C.: Osteopetrosis (Marble Bones) in an Infant, Am. J. Dis. Child. **48**:949 (Nov) 1934.

nerve, imperfect dentition, anemia and various leukemic states, and metaplasia of the bone marrow elements leading to enlargement of the liver, spleen and lymph nodes.

ETIOLOGIC AND PATHOLOGIC FACTORS [10]

The causative factor of osteopetrosis is unknown. It does, however, show a striking familial tendency and is occasionally hereditary. Parental consanguinity is apparently a factor.

The pathologic condition consists of an increase of the hard cortical bone to more than twice its normal thickness, with condensation and broadening of the bony trabeculae, obliteration of the spongiosa by the encroaching compacta and crowding of the elements of the marrow, often with replacement of the latter by fibrous tissue. When, however, marrow tissue remains, it contains active hematogenic elements. The epiphysial lines may be ragged and irregular, leading to malformations, but the periosteum is almost invariably intact. It was involved, however, in the few cases described in the literature in which the condition was complicated by syphilis. Evidently osteopetrosis is a disturbance of the endosteal and endochrondral bone metabolism—the periosteum nearly always remaining intact. There may be associated evidence of active or old rickets. The endocrine glands were involved in but a single case in the literature—that reported by Pehu and his co-workers.[8] In this case a parathyroid tumor with associated renal concretions complicated the bony involvement. Selye, working in Collip's laboratory, produced in rats a picture much like that of "marble bones" by prolonged injections of a concentrated extract of parathyroid principle. Further work along these lines is necessary.

AGE AND SEX

Osteopetrosis occurs usually in infants and young children. However, it has been diagnosed in utero [6] and in a man 68 years of age.[2] The patients whose cases have been reported are about equally divided between males and females, with a slight preponderance of males.[10]

SECONDARY MANIFESTATIONS

Multiple Fractures.—Pathologic fracture is frequent, usually occurring at right angles to the shaft of a long bone and showing a particular predilection for the femur.[2] Healing is usually prompt but in older persons there is more likely to be delay, and nonunion occurs oftener. However, the healing of fractures in malposition may lead to external deformities.

Epiphysial Deformities.—Disturbances in endochondral ossification may result in epiphysial deformities.

Retarded Development.—Children with osteopetrosis usually attain normal size unless faulty healing of numerous fractures results in a shortened stature. There is, however, some delay in the development of the secondary sex characteristics, and dentition may be late in appearing. The patients who survive infancy usually possess a good degree of intelligence.

Hydrocephalus.—Hydrocephalus is most common in infants and younger children; it is believed to be external and to result from interference with the absorption of cerebrospinal fluid,[10] but no evidence has been brought forward to substantiate this claim.

Imperfect Dentition.—This may be a constitutional defect or may in some way be related to a defect in calcium metabolism.

Atrophy of the Optic Nerve.—The thickening of the bones at the base of the skull causes a narrowing of the optic foramina. This results in pressure on the optic nerves with, first, destruction of the sensitive temporomacular bundle and central scotoma and, later, involvement of the peripheral optic fibers and complete blindness.

Anemia and Various Leukemic States.—The associated anemia is usually of the hypochromic type, and immature red cells are found in the smear of the peripheral blood. The changes in the white cells are somewhat more variable, but some type of leukemic picture is usually present. Terminally there may be evidences of aplastic anemia.

Metaplasia of the Bone Marrow Elements Leading to Enlargement of the Lymph Nodes, the Liver and the Spleen.—It was at first supposed that the enlargement of the lymph nodes, the liver and the spleen occurred in response to the need for a compensatory mechanism, after the usual site of adult hematopoiesis, i. e., the bone marrow, had become involved. However, histologic study of these extramedullary hematogenous structures has shown a surprising lack of blood-forming activity and rather an increase in the intervening connective tissue. In addition, a lack of parallelism between the condition of the bones and the degree of anemia has been noted clinically. There is, however, a certain parallelism between the degree of anemia and the enlargement of the superficial lymph nodes, the liver and the spleen. It has been suggested, therefore, that osteopetrosis is not a disease of the bony system with secondary compensatory changes in the more primitive blood-forming organizations but a disease entity involving the entire hematopoietic system.

ROENTGEN FINDINGS

The bones are unusually dense, and on roentgen examination they appear opaque, with obliteration of the shadow of the marrow cavity. Except that the distal portions of the shafts of the long bones and the centers of the flat and small bones are occasionally intact, these changes are universal, but they are most marked in the central portion of the pelvis, in the vertebral bodies, in the base of the skull, in the upper ends of the femurs and in the lower ends of both tibias and fibulas.

The sella turcica is usually narrowed and the posterior clinoid processes show a clublike thickening.

The centers of ossification usually appear at the normal time or are slightly delayed, and the union of the epiphysis with the shaft is only occasionally subject to delay. Ossification of the cranial sutures is often delayed.

Coxa vara, scoliosis, rachitic rosary deformities of the ribs and the chest and deformities of the epiphyses are observed occasionally in infants.

There is proximal and distal clubbing at the ends of the long bones —most often involving the humeri and the femurs.

Irregularity of the epiphysial line is frequently noted.

Striations consisting of alternating transverse bands of exceedingly dense and more nearly normal bone occur most often in the distal parts of the long bones. Bony trabeculae may be seen in these bands—a fact which is taken to indicate the occurrence of remissions in the disease. These changes are not usually manifest in infancy.

Fractures, both old and recent, are observed. As a rule, the roentgenogram reveals more fractures than are elicited in taking the history.

The flat bones of the pelvis and the small bones of the tarsi and the carpi may show bandlike shadows of varying density parallel to the outline of the bone. These phenomena simulate a circular defect in the bone.

CHEMICAL STUDIES

Chemical analysis of the diseased bones has revealed no marked deviation from the normal. The blood chemistry has been carefully studied in several cases, and the results have been normal unless secondary or terminal complications made the observations difficult to interpret.

PROGNOSIS

The prognosis is dependent on the age at which the disease makes itself clinically manifest [11] (being much more severe in infants) and

11. Root, J. H.: Albers-Schönberg's Disease, Am. J. Dis. Child. **49**:964 (April) 1935.

on the gravity of the secondary manifestations. There are as yet insufficient data for determining whether or not this disease is invariably progressive.

TREATMENT

Therapy should consist of precautions against trauma and the avoidance of substances, like calcium and cod-liver oil, which tend to promote bony growth. The anemia may be partially combated by the use of various iron and liver preparations. The administration of extracts of the endocrine glands has not been of benefit.

REPORT OF A CASE

G. L., a 9 year old white boy, was admitted to the children's psychiatric ward of the Bellevue Hospital on Jan. 17, 1936, because he had on several occasions attacked an older brother with a knife.

Family History.—The child's mother had married three times. George (the patient) and a brother, John, aged 10 years (the brother who had been assaulted) were children of the second marriage. Both parents were Americans of German-Irish extraction.

Past History.—The patient was a full term baby. The delivery was spontaneous and uneventful, but at birth it was noticed that he had "a huge red birth mark" covering the left side of his face and had a clubbing of the right foot. The latter was treated by exercise and massage and disappeared "when he was still an infant." As a child he had had measles, mumps and chickenpox. The mother stated that eighteen months prior to his admission to the hospital he had suffered a head trauma, after which he vomited and had headache for two days but was not kept in bed. At the age of 4 he had an inguinal hernia on the right side repaired.

Examination.—Physical examination revealed the following conditions:

The head was macrocephalic, with excessive prominence of the frontal and the parietal bosses and flattening of the occipital portion of the skull.

The fundi were normal except for excessive tortuosity of the retinal vessels.

A huge "port wine" nevus covered almost the entire left side of the face and extended up over the scalp and the left ear and down over the left side of the neck. In the center of this nevus there was a benign pigmented melanoma about 2 by 2 cm. in diameter.

Bone conduction was greater than air conduction in the left ear, and an examination of the left ear drum showed that its lower half was obscured by what seemed to be many small vessels. This was probably a nevus of the ear drum.

The left half of the soft palate and uvula were unduly red, and numerous dilated vessels could be seen through the mucous membrane.

There were a depression of the lower end of the sternum and a flaring of the lower ribs. The evidence was consistent with the existence of an old rachitic process.

The liver was palpable 2 inches (5 cm.) below the costal margin, and the lower tip of the spleen could be felt on deep inspiration.

There was a nicely healed right herniorrhaphy scar.

Neither testicle had descended into the scrotum, nor could the testicles be palpated in the inguinal canal.

The patient was otherwise normal.

In view of the facts that the contour of the boy's head was unusual and that he had had a head trauma eighteen months before his admission to the hospital, it was decided to take roentgenograms of his skull. The films were read by Dr. Lewis Friedman, chief roentgenologist of the Bellevue Hospital, who made the diagnosis of osteopetrosis.

Fig. 1.—There is no external deformity. Note the large head and the nevus on the left side of the face and the neck.

The roentgenograms revealed these changes, typical of osteopetrosis:

1. The bones were denser than normal, and the medullary structure was seen with difficulty or not at all because of the encroachment of cortical bone on the medullary cavity. These changes were universal, but they were most noticeable in the long bones, the base of the skull, the central portion of the pelvis and the vertebral bodies.

2. There was marked thickening of the bones of ths skull, particularly at the base.

3. The sella turcica was unusually narrow and showed a clublike thickening of the posterior clinoid processes.

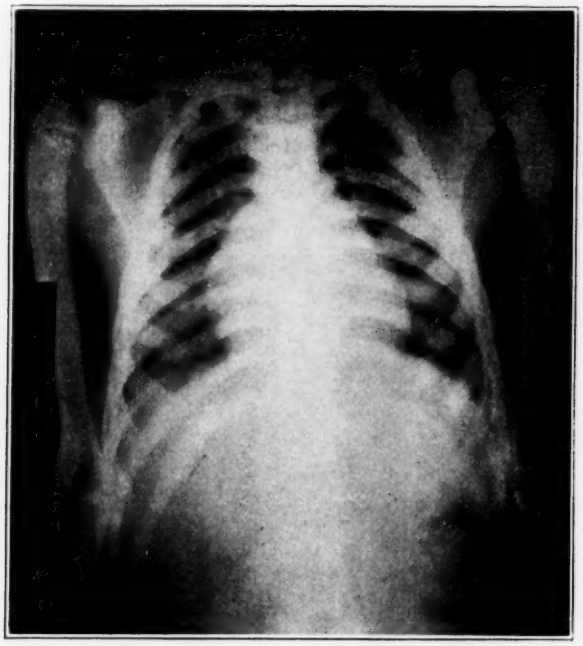

Fig. 2.—Advanced osteopetrosis at the upper ends of both humeri. Note the relative sparing of the short and flat bones.

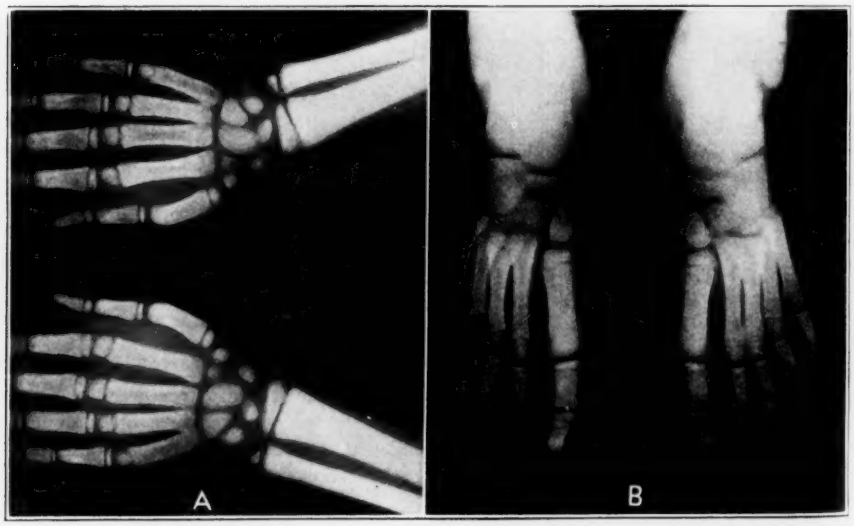

Fig. 3.—*A*, at the lower end of the bones of the forearm there is marked evidence of osteopetrosis. *B*, advanced osteopetrosis is present in both feet and about the ankle joints.

Fig. 4.—Advanced osteopetrosis of the pelvic bones and the upper ends of both femurs.

Fig. 5.—Osteopetrosis of the spinal vertebral bodies.

4. The ossification centers were slightly retarded in growth but probably within normal limits.

5. There was some clubbing at the ends of the long bones.

There were no irregularities of the epiphysial lines, no striations in the distal portions of the long bones and no pathologic fractures.

Encephalography revealed a normal ventricular system.

The intelligence quotient of the patient was 80, with a mental age of 7 years and 6 months and a specific disability in reading and spelling.

Psychiatric examination revealed that all the boy's aggressiveness was being directed against his brother John, who was one year older than he. It was felt that his attacks on the elder child were an aggressive reaction on the part of a boy both mentally and physically inferior to his elder brother.

Fig. 6.—Marked thickening of the bones at the base of the skull and narrowing of the sella turcica, with a clublike posterior clinoid process. The ventricular system is normal.

Examination of the blood gave the following results: hemoglobin, 100 per cent; red blood count, 4,650,000; white blood count, 11,850; polymorphonuclear neutrophils, 61 per cent; lymphocytes, 20 per cent; monocytes, 2 per cent; metamyelocytes I, 2 per cent; metamyelocytes II, 8 per cent; young forms, 5 per cent; eosinophils, 1 per cent; platelets, 250,000; red cell fragility test, normal result; capillary fragility test, normal result, and Wassermann reaction of the blood, negative.

Examination of fluid removed by spinal tap showed: initial pressure, 200 mm. of water; dynamics, normal; cells, 3 lymphocytes; globulin, none; total protein, 40 mg. per hundred cubic centimeters; sugar, slight trace; negative Wassermann reaction; colloidal gold curve, 0000000000.

Chemical analysis of the blood gave the following results: serum calcium 10 mg., serum phosphorus 4.1 mg., serum protein 5.7 Gm., plasma chlorides 616 mg., nonprotein nitrogen 38 mg., free cholesterol 47.6 mg., free ester 136.4 mg.

(74 per cent of total) and total cholesterol 184 mg. per hundred cubic centimeters, serum phosphatase 6.8 units, carbon dioxide 60 volumes per cent, and fixed base 150 milliequivalents.

The visual fields and acuity were normal.

The basal metabolic rate was —18 per cent and on repetition was —25 per cent.

The electrocardiogram was normal.

SUMMARY

A case of osteopetrosis ("marble bones") is presented in which there was no reason to suspect the diagnosis clinically. None of the characteristic secondary changes of the disease such as atrophy of the optic nerve, anemia, leukemia, pathologic fractures, or enlargement of the lymph nodes, were manifested. The presence of immature white blood cells in the smear of peripheral blood was the only evidence of any disturbance in hematopoiesis.

All other members of the boy's family, with the exception of the father, who could not be located, were subjected to physical and roentgen examination. They were all free from any suggestion of this disease process.

The prognosis is thought to be fairly good in this case because of the patient's age and the lack of complicating factors.

It is not felt that the osteopetrosis played any part in the problem of the boy's behavior, but it would be of interest to watch for later development of changes in the personality of the patient if his condition should progress. Bender [12] recently discussed the mechanism of psychoses and behavior problems in diseases of the bony system. She points out that the mechanism of these changes in personality "is due among other things to the discrepancy which exists between the constitutionally embedded and socially determined concept of the body image or postural model and the actual physical personality or body structure as determined by the pathological process."

The patient was a boy who apparently had a faulty "anlage" as evidenced by: (*a*) vascular anomalies of the face, the left side of the palate and the left ear drum; (*b*) inguinal hernia on the right side and clubfoot at birth; (*c*) undescended testes, and (*d*) "marble bones."

Dr. Karl M. Bowman gave me permission to report this case.

12. Bender, L.: Psychoses Associated with Somatic Diseases That Distort the Body Structure, Arch. Neurol. & Psychiat. **32**:1000 (Nov.) 1934.

Progress in Pediatrics

POLIOMYELITIS—A RÉSUMÉ

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DEFINITION

Poliomyelitis is a generalized systemic infection due to a virus, which has a predilection for the central nervous system and which sometimes produces flaccid paralysis.[1] It is also known as epidemic or acute infantile paralysis, acute wasting paralysis and Heine-Medin's disease, terms which should be discarded, since the nonparalytic form of the disease is the more common [2] and Underwood [3] described it before Heine was born.[4] Polioencephalitis is a syndrome resembling both poliomyelitis and encephalitis, and the term may signify either.

Read at the general clinical session, Southern Medical Association, twenty-ninth annual meeting, St. Louis, Nov. 20, 1935.

From the Department of Pediatrics, Duke University School of Medicine, and the Duke Hospital, Durham, N. C., with the assistance of Miss Judith Farrar, librarian at the Duke Hospital.

This information has been condensed as briefly as possible, and its sources, especially references 1 and 12 *p*, should be read for details. A thorough review of the subject and its presentation for laymen are contained in references 12 *o* and 12 *q*, respectively.

1. Landon, J. F., and Smith, L. W.: Poliomyelitis, New York, The Macmillan Company, 1934.

2. (*a*) Landon and Smith.[1] (*b*) Wickman, I.: Acute Poliomyelitis (Heine-Medin's Disease), Nervous and Mental Disease Monograph 16, New York, Nervous and Mental Disease Publishing Company, 1913. (*c*) Paul, J. R.; Salinger, R., and Trask, J. D.: "Abortive" Poliomyelitis, J.A.M.A. **98:** 2262 (June 25) 1932. (*d*) Henry, J. N., and Johnson, G. E.: Acute Anterior Poliomyelitis in Philadelphia: Comparative Study of 1916 and 1932 Epidemics, ibid. **103:** 94 (July 14) 1934. (*e*) Satos, C. M., and Rubin, M. I.: J. Pediat. **6:** 343, 1935. (*f*) Gay, C. H.: Are Transfusions Beneficial in Poliomyelitis? South. Med. & Surg. **98:**48 (Aug.) 1936. (*g*) Hunt, L. W.: A Clinical Study of Epidemic Poliomyelitis, Am. J. Dis. Child. **44:**1377 (Dec.) 1932. (*h*) Thenebe, C. L., and Cenci, V. P.: New England J. Med. **207:** 880, 1932. (*i*) Clarke, F. S.: Nebraska M. J. **17:** 283, 1932. (*j*) Gentili, A.: Riv. di clin. pediat. **30:** 1121, 1932. (*k*) Nissen, N. I.: Ugesk. f. læger **96:** 781, 1934; **97:** 1003, 1935. (*l*) Bremer, F. W.: Deutsches Arch. f. klin. Med. **173:**58, 1932. (*m*) Serum Therapy in Poliomyelitis, editorial, J. A. M. A. **103:** 262 (July 28) 1934.

3. Underwood, M.: Treatment of the Diseases of Children, ed. 4, London, J. Mathews, 1799, vol. 2, p. 84.

4. Heine, J.: Beobachtungen über Lähmungszustände der unteren Extremitäten und deren Behandlung, Stuttgart, F. H. Köhler, 1840. Medin, O.: Ueber eine Epidemie von spinaler Kinderlähmung, Verhandl. d. internat. med. Kong. **2:**37, 1891. Ruhräh, J.: J. Pediat. **3:**217, 1933.

Landry's paralysis usually, though not always, is a rapidly ascending form of poliomyelitis;[5] sometimes it is familial;[6] sometimes it is due to rabies, and occasionally it follows injections of vaccine.[7] Acute aseptic or serous meningitis[8] is very likely a nonparalytic form of poliomyelitis.

HISTORY

Evidence of poliomyelitis in Egyptian mummies of 3,700 B. C.[9] and in skeletons of vikings buried in 1,000 A. D. in Greenland demonstrates the age and widespread distribution of this disease.[10] Since its first description in 1799[11] numerous histories and summaries of it have appeared.[12]

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5. (*a*) Landon and Smith.[1] (*b*) Etienne, G.: Ann. de méd. **33**:1, 1933.

6. van der Bogert, F.: Arch. Pediat. **51**: 262, 1934.

7. Olmer, J., and Paillas, J.: Paris méd. **2**: 236, 1935.

8. (*a*) McBryde, A., and Gibert, M.: Aseptic or Serous Meningitis, to be published. (*b*) Baastrup, S.: Acta med. Scandinav. **85**:262, 1935.

9. Mitchell, J. K.: Tr. A. Am. Physicians **15**:134, 1900. Ruhräh, J.: Poliomyelitis? Am. J. Dis. Child. **43**: 195 (Jan.) 1932.

10. Aycock, W. L.: Personal communication to the author.

11. Underwood.[3] Footnote 4.

12. (*a*) Landon and Smith.[1] (*b*) Wickman.[2b] (*c*) Footnote 4. (*d*) Taylor, C. F.: Infantile Paralysis, with Its Attendant Deformities, Philadelphia, J. B. Lippincott & Co., 1867. (*e*) Sequin, E. C.: Myelitis of the Anterior Horns or Spinal Paralysis of the Adult and Child, New York, G. P. Putnam's Sons, 1877. (*f*) Collective Investigation Committee on the New York Epidemic of 1917: Epidemic Poliomyelitis, Nervous and Mental Disease Monograph 6, New York, Nervous and Mental Disease Publishing Company, 1910. (*g*) Peabody, F. W.; Draper, G., and Dochez, A. R.: A Clinical Study of Acute Poliomyelitis, Monograph 4, Rockefeller Institute for Medical Research, 1912. (*h*) Frost, W. H.: Epidemiological Studies of Acute Anterior Poliomyelitis, Bulletin 90, United States Public Health Service, Hygienic Laboratory, 1913. (*i*) Transactions of a Special Conference of State and Territorial Health Officers with the United States Public Health Service for the Consideration of the Prevention of the Spread of Poliomyelitis, Bulletin 83, United States Public Health Service, 1917. (*j*) Draper, G.: Acute Poliomyelitis, Philadelphia, P. Blakiston's Son & Co., 1917. (*k*) Ruhräh, J., and Mayer, E. E.: Poliomyelitis in All Its Aspects, Philadelphia, Lea & Febiger, 1917. (*l*) Lavinder, C. H.; Freeman, A. W., and Frost, W. H.: Epidemiologic Studies of Poliomyelitis in New York City and the Northwestern United States During 1916, Bulletin 91, United States Public Health Service, 1918. (*m*) Caverly, C. S., and others: Infantile Paralysis in Vermont, 1894-1922, Burlington, Vt., State Department of Public Health, 1924. (*n*) MacAusland, W. R.: Poliomyelitis with Especial Reference to the Treatment, Philadelphia, Lea & Febiger, 1927. (*o*) Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Organized by Jeremiah Milbank, Baltimore, Williams & Wilkins Company, 1932. (*p*) Special Committee on Poliomyelitis: Practical Suggestions on Poliomyelitis, Chicago, American Medical Association, 1934. (*q*) Draper, G.: Infantile Paralysis, New York, D. Appleton-Century Company, Inc., 1935. (*r*) Ruhräh, J.: J. Pediat. **3**: 217 and 765, 1933. (*s*) Wilder, T. S.; Scott, J. P.; Stokes, J., Jr.; Lyon, J. M., and Wagoner, G.: M. Clin. North America **18**: 1, 1934.

INCIDENCE, SUSCEPTIBILITY AND DISTRIBUTION

Numerical.—It has been estimated that 1 child in every 1,000 probably will have paralytic manifestations of the disease at some time during his life.[10] In the worst epidemics, which occur irregularly, 1 person in 500 contracts poliomyelitis.[1] If cases of the nonparalytic and suspected abortive types are included, the epidemic incidence may be 1 in 10 for all children.[2c] For the past nine years an annual average of 7,000 cases of poliomyelitis has been reported for the United States, in contrast with a total of 28,000 cases of smallpox.[13] Forty per cent of all crippling is said to be due to poliomyelitis, as compared with 30 per cent caused by tuberculosis.[14]

Geographic, Seasonal and Climatic.—The disease has appeared at some time in every area of the world;[1] from 1841 to 1911, 149 epidemics were listed.[12k] It is more prevalent in rural localities than in cities.[15] In the southern states the average annual incidence is one-third as high as in the New England states;[1] however, the annual rate in North Carolina increased ninefold in 1935.[15d] Epidemics of the disease are rare in warm climates, and the paralytic manifestations become less frequent as the tropics are approached, but, paradoxically, the incidence of paralysis is highest during the summer months, usually reaching its peak late in August or early in September.[16] Sometimes a lower preliminary peak is attained in March or April.[16g] In the 1935 outbreak the peak was reached on June 29 in North Carolina and on August 3 in Virginia.[17] In California the peak is in October, and in

13. Williams, R. C.: Cases reported to the United States Public Health Service, 1926-1934, personal communication to the author.

14. Harris, R. I., quoted in Transactions of the International Society for Crippled Children, Am. J. Dis. Child. **44:** 908 (Oct.) 1932.

15. (*a*) Lovegren, E.: Acta psychiat. et neurol. **6:** 327, 1931. (*b*) McQuarrie, Irvine: Personal communication to the author. (*c*) Ullrich, O.: Ztschr. f. Kinderforsch. **41:** 357, 1933. (*d*) Root, A. S.: South. M. J. **29:** 184, 1936. (*e*) Schultz, E. W.: J. Pediat. **1:** 358, 1932 (*f*) Kramer, S. D.: Immunity to Poliomyelitis in the General Population, J. A. M. A. **99:** 1048 (Sept. 24) 1932. (*g*) Paul, J. R., and Trask, J. D.: J. Exper. Med. **61:** 447, 1935. (*h*) Schultz, E. W., and Gebhardt, L. P.: California & West. Med. **43:** 111, 1935. (*i*) Active Immunization in Poliomyelitis, current comment, J. A. M. A. **105:** 1527 (Nov. 9) 1935. (*j*) Reynolds, C. V., and Knox, J. C.: Am. J. Pub. Health **26:** 95, 1936. (*k*) Gilliam, A. G., and Onstott, R. H.: ibid. **26:**113, 1936; Pub. Health Rep. **51:**160, 1936.

16. (*a*) Wickman.[2b] (*b*) Satos and Rubin.[2e] (*c*) Aycock.[10] (*d*) Footnote 12*f*. (*e*) Toomey, J. A., and Lipson, H. A.: J. Pediat. **1:** 739, 1932. (*f*) Toomey, J. A., and August, M. H.: ibid. **1:** 601, 1932. (*g*) Aycock, W. L., and Eaton, P.: Am. J. Hyg. **4:** 356, 1924. (*h*) Toomey, J. A., and August, M. H.: Poliomyelitis: Comparison Between the Epidemic Peak and the Harvest Peak, Am. J. Dis. Child. **46:** 262 (Aug.) 1933.

17. Riggin, I. C.: Am. J. Pub. Health **26:** 98, 1936.

New Zealand, in February or March.[1] There are some indications that the nonparalytic immunizing form of the disease may be frequent during the winter.[10] Apparently there is no correlation between atmospheric temperature, rainfall and the occurrence of epidemics of poliomyelitis.[16f]

Age.—The greatest incidence of the disease is in children between the ages of 2 and 6 years,[18] but the condition may occur in the newborn [18p] and in persons of middle age.[19] In country districts the average age of the patients is higher than in cities.[15c] Frequency of exposure seems to determine the degree of susceptibility.[18g]

Race and Sex.—Poliomyelitis apparently most frequently attacks good-looking, well developed males.[20] A study of 622 cases in North Carolina in 1935 showed that the disease was only two-thirds as common among Negroes as it was among white persons, a proportion which has been found elsewhere;[21] but among the few Indians affected it was four times as frequent.[15d] Among the white patients in North Carolina the incidence was one-third higher in males than in females, as in other outbreaks,[22] while among Negroes the incidence in males was slightly lower and among Indians only half as high as in females.[15d]

Constitution.—The highest incidence of poliomyelitis is among well nourished persons[1] with high, narrow palates,[23] widened interpupillary spaces and other measurements suggesting a "thymic" constitution and a deficiency of the pituitary gland, gonads and adrenal cortex,[24] as well as a greater absorbing surface for nasal infection. With children it is more difficult to demonstrate the relation of physical characteristics to

18. (*a*) Landon and Smith.[1] (*b*) Henry and Johnson.[2d] (*c*) Underwood.[3] (*d*) Ullrich.[15e] (*e*) Root.[15d] (*f*) Hecht, B. C.: M. J. & Rec. **135:** 19, 1932. (*g*) Kramer, B.: New York State J. Med. **32:** 855, 1932. (*h*) Waltner, K.: Arch. f. Kinderh. **100:** 147, 1933. (*i*) Nelis, P., and Geens, J.: Rev. belge sc. méd. **5:** 317, 1933. (*j*) Guttman, L.: Med. Klin. **29:** 939, 1933. (*k*) Gentili A.: Riv. di clin. pediat. **31:** 24, 1933. (*l*) Peck, H. T.: New York State J. Med. **32:** 854, 1932. (*m*) Steigrad, J.: M. J. Australia **1:** 785, 1932. (*n*) Wells, M. W.: New York State J. Med. **32:** 393, 1932. (*o*) Rankin, W. S.: Bull. North Carolina Bd. Health **31:** 288, 1916. (*p*) Lance, M.: Bull. Soc. de pédiat. de Paris **31:** 229, 1933. (*q*) Aycock, W. L.: Am. J. Pub. Health **24:** 433, 1934. (*r*) Jungeblut, C. W., and Engle, E. T.: Susceptibility Problems in Poliomyelitis, Am. J. Dis. Child. **43:** 523 (Feb.) 1932.

19. Landon and Smith.[1] Root.[15d]

20. (*a*) Borovsky, M. P., in discussion of papers on poliomyelitis, Am. J. Dis. Child. **44:**1380 (Dec.) 1932. (*b*) Taillens, M.: Bull. Soc. de pédiat. de Paris **31:**304, 1933.

21. Henry and Johnson.[2d] Hecht.[18f] Borovsky.[20a]

22. (*a*) Landon and Smith.[1] (*b*) Satos and Rubin.[2e] (*c*) Geiger, J. C., and Gray, J. P.: J. Prev. Med. **6:**145, 1932.

23. Thelander, H. E., and Pryor, H. B.: Arch. Pediat. **50:**749, 1933.

24. Draper, G.: Am. J. M. Sc. **184:**111, 1930.

the incidence of poliomyelitis.[25] Susceptibility may sometimes run in families.[26] Since the urine of pregnant women and epinephrine neutralize the poliomyelitis virus, the hypothesis has been advanced that susceptibility to this disease may be due to endocrine deficiency.[27]

Blood Types.—Although the studies may not have statistical significance, few persons with group A B or group B blood have been found to have poliomyelitis,[28] and the titer of the neutralizing power of the serum of convalescent patients and normal adults is reported as lowest for persons who have group O blood.[27]

Animals.—During epidemics, illness among horses, dogs and chickens is said to increase, with a high incidence of paralysis among chickens.[29] However, the pathogenicity of the poliomyelitis virus seems to be restricted to man and certain monkeys.[15e]

ETIOLOGY

The proof is conclusive that the infectious agent of poliomyelitis is a virus.[30] The physical properties of this virus have been thoroughly studied.[31] Its presence can be determined by inoculation of monkeys, and antibodies to it can be titrated by neutralization tests.[32] A toxic factor has been found in the stools and urine of patients with poliomyelitis and inoculated monkeys, which can be neutralized by horse

25. Levine, M. I.; Neal, J. B., and Park, W. H.: Relation of Physical Characteristics to Susceptibility to Anterior Poliomyelitis, J. A. M. A. **100**:160 (Jan. 21) 1933.

26. Aycock, W. L.: West Virginia M. J. **30**:481, 1934.

27. Jungeblut, C. W.: J. Immunol. **27**:17, 1934. Jungeblut, C. W.; Meyer, K., and Engle, E. T.: ibid. **27**:43, 1934.

28. Jungeblut, C. W., and Smith, L. W., Jr.: J. Immunol. **23**:35, 1932. Smith, L. W., Jr., and Jungeblut, C. W.: ibid. **23**:1, 1932. Shaw, E. B.; Thelander, H. E., and Kilgariff, K.: J. Pediat. **1**:346, 1932. Hatsky, K.: München. med. Wchnschr. **80**:1973, 1933.

29. Krause, P.: München. med. Wchnschr. **80**:1159, 1933.

30. Schultz.[15e] Flexner, S., and Lewis, P. A.: The Transmission of Acute Poliomyelitis to Monkeys, J. A. M. A. **53**:1639 (Nov. 13) 1909. Landsteiner, K., and Popper, E.: Wien. klin. Wchnschr. **21**:1830, 1908. Leiner, C., and von Wiesner, R.: ibid. **22**:1698, 1909. Römer, P.: München. med. Wchnschr. **56**: 2505, 1909.

31. (*a*) Landon and Smith.[1] (*b*) Jungeblut, J.: J. Bact. **27**:81, 1934. (*c*) Gordon, W. S.: Brit. M. J. **1**:885, 1934. (*d*) Wayson, N. E.; Leake, J. P., and Stimson, A. M.: Bulletin 111, United States Public Health Service, Hygienic Laboratory, 1918. (*e*) Flexner, S.: J. Exper. Med. **63**:209, 1936. (*f*) Flexner, S., and Noguchi, H.: Experiments on the Cultivation of the Virus of Poliomyelitis, J. A. M. A. **60**:362 (Feb. 1) 1913; J. Exper. Med. **18**:461, 1913. (*g*) Eberson, F.: J. Lab. & Clin. Med. **18**:565, 1933. (*h*) Hurst, E. W.: J. Path. & Bact. **34**:331, 1931.

32. Levaditi, C., and Landsteiner, K.: Compt. rend. Soc. de biol. **68**:311, 1910.

serum.[33] A double etiology of a virus and organisms in the stools has been suggested,[34] but, like the occasionally resurrected theory that the streptococcus is the cause of poliomyelitis,[35] that theory is sinking into oblivion.

PATHOLOGIC PROCESS

In the acute state the reticulo-endothelial system is always involved;[36] the thymus is congested, and there is acute follicular necrosis of the germinal centers of the spleen and of the intestinal lymphoid structures, but only to a slight extent of the lymph nodes of the periphery, mediastinum and mesentery. The tonsils usually are hyperplastic. Petechial hemorrhages are found in the fundus of the stomach.[1] The distinctive degenerative lesion of the disease is found most commonly in the ganglion cells of the lower motor neurons in the lumbar and cervical enlargements of the spinal cord.[37] The axons show demyelini-

33. (*a*) Toomey, J. A.: Neutralizing Value of Various Substances Against Lethal Doses of (A) Stool Emulsions from Patients with Poliomyelitis and (B) Colon Paratyphoid Organisms, Am. J. Dis. Child. **48**:1284 (Dec.) 1934; (*b*) J. Prev. Med. **6**:379, 1932; Jahrb. f. Kinderh. **143**:353, 1934. (*c*) Toomey, J. A., and von Oettingen, W. F.: An Enterodepressant Factor in the Stools and Spinal Cords of Monkeys Infected with Poliomyelitis, Am. J. Dis. Child. **48**:30 (July) 1934. (*d*) Clark, P. F.; Roberts, D. J., and Preston, W. S., Jr.: J. Prev. Med. **6**:47, 1932. (*e*) Toomey, J. A.: Toxicity of Organs of Animals Dying After Injections of Emulsions of Stools of Patients with Poliomyelitis, Am. J. Dis. Child. **50**:1173 (Nov.) 1935; Poliomyelitis: II. The Bulbar Type, ibid. **50**:1362 (Dec.) 1935.

34. Toomey.[33b] Synergistic Etiology of Poliomyelitis, editorial, J. A. M. A. **103**:757 (Sept. 8) 1934.

35. Mathers, G.: Some Bacteriologic Observations on Epidemic Poliomyelitis, J. A. M. A. **67**:1019 (Sept. 30) 1916. Olitsky, P. K.; Rhoads, C. P., and Long, P. H.: Relation of Streptococci to the Spinal Fluid in Experimental Poliomyelitis, ibid. **92**:1725 (May 25) 1929. Rosenow, E. C.: Proc. Soc. Exper. Biol. & Med. **27**:444, 1930. Cooper, M. L.: Studies in the Etiology of Poliomyelitis, Am. J. Dis. Child. **43**:776 (March) 1932. Rosenow, E. C.: J. Infect. Dis. **50**:377, 1932.

36. Burrows, M. T.: Is Poliomyelitis a Disease of the Lymphatic System? Arch. Int. Med. **48**:33 (July) 1931.

37. (*a*) Landon and Smith.[1] (*b*) Footnote 12*p*. (*c*) Covell, W. P.: Nerve Degeneration in Poliomyelitis: V. Correlation of Fiber Changes in Nerves with Cellular Changes in the Spinal Cord, Arch. Neurol. & Psychiat. **28**:1056 (Nov.) 1932. (*d*) Brodie, M.: Cerebral Involvement in Acute Anterior Poliomyelitis, Am. J. Dis. Child. **48**:57 (July) 1934. (*e*) Marinesco, G., and Draganesco, S.: Rev. neurol. **1**:1, 1932. (*f*) Levaditi, C.; Kling, C., and Horms, G.: Compt. rend. Soc. de biol. **112**:43, 1933. (*g*) Mayerhoff, E.: Arch. f. Kinderh. **101**:160, 1934. (*h*) The Gastro-Intestinal Tract and the Autonomic Nervous System in Poliomyelitis, editorial, J. A. M. A. **103**:840 (Sept. 15) 1934. (*i*) Toomey, J. A.: Science **82**:200, 1935.

zation; if the axis-cylinders are destroyed, the paralysis is permanent. There may be extensive necrosis of the substance of the cord,[1] with loss of minerals in the nerve cells,[38] and capillary hemorrhages and interstitial cellular infiltration occur about the vessels.[1]

PORTAL OF ENTRY AND MODE OF INFECTION

The neurotropic virus enters through the olfactory mucosa and cribriform plate and travels along the nerves from the upper olfactory centers to the anterior horns of the spinal cord, where it produces its most marked effects.[39] The proof of nasal infection seems conclusive.[40] A gastro-intestinal portal of entry and passage of the virus along the vagus and the seventh nerve also have been suggested,[41] but are not seriously regarded.

SYMPTOMS AND SIGNS

As may be seen in table 1, fever and headache are the most common and may be the only symptoms.[42] Without rigidity of the spine and back, the chance of paralysis is slight.[10] All present figures on morbidity and mortality rates, percentage of paralysis, effects of various types of treatment, etc., depend on the number of cases of "mild" involvement included in the series. Before sound clinical and therapeutic progress is possible, a simple diagnostic test is necessary;[43] fortunately, or unfortunately, most of the patients who have only fever and headache will not submit to routine lumbar punctures. If paralysis does not develop, a diagnosis of abortive poliomyelitis often is made, which is erroneous, for it presupposes that paralysis is essential for the true disease. The percentage of patients with poliomyelitis in whom the injury has not been sufficient to produce paralysis is unknown; estimates of from 10 to 86 per cent have been made.[44] This type is said to occur

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38. Patton, W. E.: Am. J. Path. **10**:615, 1934.

39. (*a*) Landon and Smith.[1] (*b*) Schultz.[15e] (*c*) Marinesco and Draganesco.[37e] (*d*) Faber, H. K.: Medicine **12**:83, 1933; Science **82**:42, 1935.

40. Landon and Smith.[1] Wayson and others.[31d] Clark and others.[33d] Schultz, E. W., and Gebhardt, L. P.: Proc. Soc. Exper. Biol. & Med. **31**:728, 1934. Lovett, T.: Internat. Clin. **2**:16, 1934. Lennette, E. H., and Hudson, N. P.: Proc. Soc. Exper. Biol. & Med. **32**:1444, 1935.

41. Toomey.[33e] Levaditi and others.[37f] Mayerhoff.[37g] Footnote 37*h*. Toomey.[37i]

42. Henry and Johnson.[2d] Satos and Rubin.[2e] Gay.[2f] Hunt.[2g]

43. Kolmer, J. A., and Rule, A. M.: J. Immunol. **29**:175, 1935. Kolmer, J. A.; Klugh, George, Jr., and Rule, A. M.: ibid. **29**:191, 1935. Kolmer, J. A., and Rule, A. M.: ibid. **29**:199, 1935.

44. (*a*) Footnote 2. (*b*) London, A. H., and Roberts, B. W., Jr.: On the Poliomyelitis Epidemic in North Carolina, Tr. M. Soc. North Carolina **83**:460, 1936. (*c*) Waddell, W. W., Jr., and Purcell, C. W.: Am. J. Pub. Health **26**:104, 1936.

more frequently among older children and adults.[45] It has also been observed in monkeys inoculated with the virus.[46]

In the patients who later become paralyzed the interval between the onset of symptoms and paralysis is called preparalytic, which is misleading, for the term represents a stage before the injury to the neurons has progressed sufficiently to produce paralysis and not a stage before the nerves are affected.[47] The average length of this interval is four days.[48] In monkeys the period between the inoculation with the virus and the appearance of paralysis ranges from three to thirty-two days, with an average of from eight to nine days.[49]

TABLE 1.—*Symptoms and Signs in Poliomyelitis*

	Percentage of Patients Having Each Symptom and Sign*					
Symptom or Sign	368 Cases, Chicago, 1931 [2f]	270 Cases, Hartford, Conn., 1931 [2g]	728 Cases, Philadelphia, 1932 [2c]	100 Cases, Philadelphia, 1932 [2d]	111 Cases, Charlottesville, Va., 1935 [44d]	24 Cases, Durham, N. C., 1935 [2e]
Fever	83	87	92	91	54 (on examination)	83
Headache	37	70	66	47	75	63
Vomiting	56	45	48	37	56	50
Anorexia	..	53	..	..	..	42
Infection of upper respiratory tract	..	37	2	64	..	8
Stiff neck	..	93	50	65	38	42
Rigid spine	..	83	24	39	38	42
Paralysis	68	65	62	48	22	50
Pain	36	..	37	66	27†	..
Irritability	..	52	33	..	..	4
Drowsiness	..	13	19	59	15	24
Hyperesthesia	..	..	27	63	9	..
Constipation	9	2	16	40	..	..
Diarrhea	5	2	15	10	9	4
Chills	..	..	15	..	..	..
Kernig sign	..	..	7	..	..	..
Muscular twitching	..	..	7	..	..	..
Babinski sign	..	..	3	..	..	..
Convulsions	2	..	4	10	2	..

* The following symptoms occurred in less than 1 per cent of the cases: delirium, coma, urinary retention,[1] fecal and urinary incontinence [52b] and photophobia.
† In 18 per cent pain was in the abdomen; in 9 per cent, in the extremities.

After an incubation period of from six to twenty days (average, one week) [50] the course of the so-called classic poliomyelitis (sporadic and epidemic types are identical [51]) has been divided into four stages, any of which may be absent. The first phase has been called the systemic,[1] cerebral or diencephalic phase.[39d] The infection is localized in the olfactory bulb, hypothalamus and thalamus (midbrain and medulla).

45. Bremer.[21] Footnote *2m*.
46. Harmon, P. H.; Shaughnessy, H. J., and Gordon, F. B.: J. Prev. Med. **5**:115 and 139, 1931.
47. Walshe, F. M. R.: Brit. M. J. **2**:1197, 1933.
48. Landon and Smith.[1] Satos and Rubin.[2e] Bremer.[21]
49. Flexner, S., and Amoss, H. L.: J. Exper. Med. **25**:499, 1917.
50. Aycock, W. L., and Luther, E. H.: J. Prev. Med. **3**:103, 1929.
51. Landon, J. F.: J. Pediat. **5**:1, 9, 16, 29 and 33, 1934.

The symptoms, which may last from a few hours to several days, may be any of the following: fever, headache, drowsiness, irritability, rigors, sweating, hyperesthesia, anxiety, vomiting, diarrhea, constipation, coryza, sore throat and cough. The second phase follows the first after a latent period varying from a few hours to several days and is described as the stage of posterior poliomyelitis, the lower sensory stage [39d] or the period of invasion of the central nervous system.[1] The inflammatory process is spreading from the thalamus through the spinothalamic tract to the posterior horns of the cord and posterior root ganglions. The associated symptoms and signs may be localized pain and tenderness, stiff neck, rigid spine (which may persist for three or four weeks), a positive Kernig, Brudzinski or Oppenheim sign, convulsions, delirium and increased tendon reflexes.[52] No further symptoms may occur, or, after another interval, which usually is short but may be as long as twelve days, the third phase or stage, anterior poliomyelitis, or the lower motor stage, may begin. The anterior horns and columns of Clarke

TABLE 2.—*Location of Paralysis in Patients with Poliomyelitis*

	Percentage of Patients					
Location	868 Cases, Sweden, 1905 [2a]	123 Cases, Pisa, Italy, 1924-31 [18k]	728 Cases, Philadelphia, 1932 [2c]	100 Cases, Philadelphia, 1932 [2d]	24 Cases (Among 111), Charlottesville, Va., 1935 [44d]	24 Cases, Durham, N. C., 1935 [2e]
One or both legs (only)	41	62	23.5	17	10	33.3
One or both arms (only)	9	10	12.2	8	5	21.0
Arms and legs	18	12	....	11	5	....
Legs and trunk	10	..	....	..	..	....
Cranial nerves (bulbar)	7	16	....	12	5	4.0

are implicated,[39d] and the following signs may be present: tremors, twitching, ataxia, weakness, diminution or loss of reflexes, diminished electrical reactions, anesthesia, urinary and fecal incontinence [52b] and flaccid paralysis, the last usually being incomplete. The quadriceps, tibialis anticus and peroneal group of muscles are most frequently attacked. The deltoid is the muscle of the arm most commonly involved.

The bulbopontile type of poliomyelitis, in which the cranial nerves, usually only on one side, are involved (ptosis, squint, etc.), comprises from 4 to 16 per cent of the cases in which there is paralysis (table 2). This type is said to be more common in sporadic than in epidemic cases.[53] The facial nerve is most frequently implicated; probably in many of the sporadic cases of Bell's palsy this condition is due to poliomyelitis. The glossopharyngeal nerve is next most commonly attacked, with

52. (*a*) Faber.[39d] (*b*) Toomey, J. A.: Intestine and Urinary Bladder in Poliomyelitis, Am. J. Dis. Child. **45**:1211 (June) 1933; Some Reflex Changes in Poliomyelitis, ibid. **46**:730 (Oct.) 1933.

53. Bamatter, F.: Arch. f. Kinderh. **101**:193, 1934.

nasal regurgitation and inability to swallow,[1] which, though it usually is over in one week, may last from a few hours to seventy-one days.[54] Respiratory paralysis is relatively rare in cases of bulbopontile involvement.

If the patient does not die, the fourth phase, or stage of recovery or remission, may follow within the next two years [1] or within five years.[3] The infection dies out, the undestroyed cells recover and the inflammation subsides.[39d] The paralysis may diminish, and pain and tenderness may reappear temporarily. If the paralysis is permanent, wasting of the muscles, loss of weight, ataxia, changes in temperature of the part and crippling and contracture (unless corrected) develop. Comparatively few patients are permanently bedridden.

The type of onset apparently varies in different epidemics, headache, rigid spine,[55] pain in the muscles [56] or meningitic,[2h] gastro-intestinal or respiratory symptoms being the most prominent first symptoms.[1] Obviously, with such a variety of symptoms which vary in different outbreaks (table 1), no universal rule of diagnosis is applicable; the possibility of poliomyelitis should always be considered. As the present methods of therapy during the acute stage seem to be valueless, an accurate diagnosis is not as essential as it is, for example, in diphtheria or meningitis. As a matter of fact, disturbing the patient during the acute stage, especially by making him walk, in an overzealous hunt for slight signs of weakness, may be harmful. The chief therapeutic need at this stage is complete rest in bed.[12p] The most important objective in the examination for paralytic symptoms in poliomyelitis, the details of which are described elsewhere,[12p] is not to diagnose the disease but to ascertain just which groups of muscles are weak and need rest and protection against stretching by opposing muscles. Later, after complete subsidence of the acute symptoms, the activity, rest and position of each part of the body for every hour of the day as well as for the periods of active training of the muscles should be controlled.[12p]

PROGNOSIS

The mortality and the percentage of paralysis, as stated previously, depend on the number of cases of the nonparalytic type included in the figures. In one city in North Carolina in 1935, lumbar punctures were done on every patient with fever and headache; as a result, many cases of "mild" poliomyelitis were discovered, and naturally the mor-

54. Brahdy, M. B., and Lenarsky, M.: Difficulty in Swallowing in Acute Epidemic Poliomyelitis, J. A. M. A. **103**:229 (July 28) 1934.

55. (*a*) Baastrup, S.: Ugesk. f. læger **96**:759, 1934. (*b*) Torian, O. N., and Winters, M.: J. Pediat. **1**:326, 1932. (*c*) Rosenberg, C.: Arch. Pediat. **49**:705, 1932. (*d*) Wieland, E.: Jahrb. f. Kinderh. **143**:321, 1934.

56. Langstein, L.: Kinderärztl. Praxis **3**:537, 1932.

tality and the percentage of paralyzed patients appeared much lower[57] than in a series of cases in which lumbar puncture was done only if the patient's symptoms were definite.[15d] Published mortality figures range from zero to 78 per cent,[58] the lowest being for children between the ages of 1 and 7 years.[1] Practically all the deaths are due to respiratory failure (intercostal or diaphragmatic paralysis) or to bulbar involvement, especially if the patient has been placed in a respirator.[59] The majority of the deaths occur from the third to the eighth day after the onset.[1] In an average epidemic the percentage of patients in whom any form of paralysis develops usually is much less than 50 and may be as low as 10,[44c] and of this percentage the proportion permanently or seriously crippled is small.[10] The tendency is to recover; much of the permanent paralysis usually is due to neglect or improper management.[12r] The lowest percentge of paralysis is in patients who are placed in bed immediately after the onset[2f] of symptoms. Recovery of the weight-bearing muscles of the legs is less sure than of the muscles of the arm, though the deltoid, which is constantly stretched by the weight of the arm—unless supported—is slow to improve.[12p] The fate of 605 patients who had survived the acute stage was investigated six months later. Forty-three and eight-tenths per cent were normal; the condition of 37.6 per cent was good, fair or poor; 3.4 per cent had a trace of paralysis; 2 per cent were totally paralyzed, and 13.2 per cent were dead.[2d]

LABORATORY TESTS

As previously stated, a simple diagnostic test is badly needed.[43] At present changes in the spinal fluid are the best criteria, but they are none too good. In cases of suspected poliomyelitis it is most important to verify, by lumbar puncture and spinal fluid smears and cultures, the presence or absence of treatable meningitis. Cisternal punctures apparently are dangerous in cases of poliomyelitis.[1]

Spinal fluid cell counts range from zero to 1,500, with more than half being between 50 and 100 cells.[60] The predominating cell usually is

57. Gay.[2f] London and Roberts.[44c]

58. (*a*) Landon and Smith.[1] (*b*) Wickman.[2b] (*c*) Gay.[2f] (*d*) Ruhräh.[12k] (*e*) Root.[15d] (*f*) Geiger and Gray.[22c] (*g*) London and Roberts.[44b] (*h*) Brink, C. D.: South African M. J. **8**:560, 1934. (*i*) Committee on Poliomyelitis: Ugesk. f. læger **97**:837, 1935. Christensen, R. E.: ibid. **97**:855, 1935. (*j*) Brown, E. G.: Pub. Health Rep. **47**:1899, 1932.

59. (*a*) Landon and Smith.[1] (*b*) Footnote 12*p*. (*c*) Brahdy, M. B., and Lenarsky, M.: Treatment of Respiratory Failure in Acute Epidemic Poliomyelitis, Am. J. Dis. Child. **46**:705 (Oct.) 1933. (*d*) Shaw, E. B.; Thelander, H. E., and Limper, M. A.: California & West. Med. **35**:5, 1931. (*e*) Wilson, M. J.: New England J. Med. **206**:887, 1932.

60. (*a*) Landon and Smith.[1] (*b*) Gay.[2f] (*c*) Hunt.[2g] (*d*) London and Roberts.[44b] (*e*) Langstein.[56] (*f*) Kessel, J. F.; Hoyt, A. S., and Fisk, R. T.: Am. J. Pub. Health **24**:1215, 1934.

the lymphocyte or large mononuclear, although the percentage of polymorphonuclears may be the highest, especially during the first few days.[1] It is said that the prognosis is worst in patients with high cell counts,[61] but some definitely paralyzed patients do not have an increase in the number of cells.[62]

The protein content of the spinal fluid usually, though not always, is increased.[63] This elevation is in both the globulin and the albumin fraction, in a variable ratio.[64] The protein content and cell count show little correlation.[1] The increase in globulin may remain for fifty days, but the fibrinogen disappears quickly.[65]

Determination of the sugar content of the spinal fluid is not always a reliable diagnostic test;[8b] the content may be normal[66] or increased, especially in the bulbar type.[67] The diastase content, which may be increased in severe poliomyelitis, has no relation to the sugar content.[68] In animals inoculated with the poliomyelitis virus the blood sugar content is not changed, but the sugar tolerance is reduced.[69]

The colloidal gold and mastic spinal fluid curves usually are of the syphilitic or the meningitic[70] zone type.

The white blood cell count usually is increased, with a diminution of lymphocytes[1] or a slight increase in neutrophils,[71] although a normal count or leukopenia is common.

DIFFERENTIAL DIAGNOSIS

Since the clinical picture of poliomyelitis changes during the four phases of the disease, the conditions with which it is confused depend on the stage. Because of similarity to the first stage, every case of infection of the upper respiratory tract and of gastro-enteritis, especially during epidemics of poliomyelitis, should be viewed with suspicion.[1] During the second stage the following conditions should be differentiated: meningitis, especially tuberculous (although the meningococcic,

61. Landon and Smith.[1] Footnote 12*i*.

62. Landon and Smith.[1] Footnote 55. Kissel.[60f] Levinson, S. O.: J. Pediat. **1**:337, 1932.

63. Landon and Smith.[1] Footnote 55.

64. (*a*) Landon and Smith.[1] (*b*) Footnote 55. (*c*) Plant, F.: München. med. Wchnschr. **79**:1548, 1932.

65. Kramar, E., and Liszka, I.: Monatschr. f. Kinderh. **60**:136, 1934.

66. Landon and Smith.[1] Footnote 12*p*. Plant.[64c]

67. Landon and Smith.[1] Ghio, A., and Ranno, A.: Riv. di clin. pediat. **30**: 1159, 1932.

68. Eckardt, F.: Jahrb. f. Kinderh. **142**:303, 1934.

69. Jungeblut, C. W., and Resnick, R.: Blood Sugar Levels and Dextrose Tolerance Test in Experimental Poliomyelitis, Am. J. Dis. Child. **51**:91 (Jan.) 1936.

70. Landon and Smith.[1] London and Roberts.[44c] Plant.[64c]

71. Plum, P.: Ugesk. f. læger **97**:1012, 1935.

influenzal, pneumococcic, streptococcic and serous forms, the type due to Brucella[8] and other forms occasionally resemble poliomyelitis), meningismus, encephalitis, epilepsy, influenza, pneumonia, serum disease, typhoid or paratyphoid fever, arthritis, rheumatic fever, rheumatic torticollis, cervical abscess, bacteremia, appendicitis,[72] tetanus, tetany, trauma, alkalosis and asphyxia. During the paralytic, or third stage the following diseases must be considered: peripheral neuritis, beriberi, myatonia congenita, muscular atrophy or dystrophy, cerebellar ataxia, cerebral degeneration, spastic diplegia, the pseudoparalysis of rickets, scurvy, syphilis, injuries to or infections of bones, joints or muscles, lead poisoning, diphtheria and croup (often confused with the bulbar type of poliomyelitis), hysteria, facial paralysis due to a

TABLE 3.—*Diseases Mistaken for Poliomyelitis in 113 of the 1123 Cases in Which the Patient Was Admitted with a Diagnosis of Poliomyelitis to the Willard Parker Hospital in 1931*[74]

Final Diagnosis*	Number of Cases
Infection of the upper respiratory tract, tonsillitis and otitis media	27
Dysentery and nutritional disturbance	14
Meningitis (tuberculous and purulent)	9
Pneumonia	9
No diagnosis	8
Trauma	6
Arthritis (including epiphysitis and synovitis)	6
Osteomyelitis and deep abscesses	5
Neurosis	4
Cerebral hemorrhage or arteriosclerosis	4
Rheumatic fever	3
Neuritis	2
Torticollis	2
Disease of the serum	2

* The following were each diagnosed in one case: appendicitis, Bell's palsy, cervical adenitis, encephalitis, epidural abscess, epilepsy, myelitis, myositis, syphilis, tetanus, typhoid fever and vaccination.

local cause, transverse myelitis, spinal or cerebral tumor, abscess, hemorrhage, embolism, thrombosis and syringomyelia.[73] In table 3 are listed the conditions mistaken for poliomyelitis during one epidemic.[74]

TREATMENT

General Care.—Absolute rest in bed in the position the patient would be in if standing erect,[12r] or in that of greatest comfort, good nursing and quiet surroundings are essential during the acute stage.[75] A fracture board may be necessary to prevent sagging of the mattress. Pain should be relieved by sedatives, hot applications or immersion of

72. Hobart, M. H.: Illinois M. J. **61**:518, 1932.

73. (*a*) Landon and Smith.[1] (*b*) Landon.[51] (*c*) Sherwood, D. W.: New England J. Med. **207**:571, 1932. (*d*) Brahdy, M. B., and Lenarsky, M.: Differential Diagnosis of Acute Poliomyelitis, J. A. M. A. **102**:1358 (April 28) 1934.

74. Landon.[51] Brahdy and Lenarsky.[73d]

75. Landon and Smith.[1] Footnote 12*p*.

the affected limb in a tepid bath.[75] The patient should be moved and disturbed as little as possible. Orthopedic treatment, the details of which are described elsewhere,[76] is desirable from the onset. If the slightest weakness develops in any muscles, in order to protect them and to prevent stretching, contracture and deformity, the affected limb should immediately be placed at complete relaxation and rest in an overcorrected or neutral position and should be held by splints, braces or, preferably, by comfortable light weight plaster casts; the opposing muscle group, especially, must be watched for weakness. The part should be kept warm by hot water bottles and bed clothing supported by a cradle.[12p] If there is a choice, the muscles which are most important for an erect position should be protected, e. g., the hip extensors, the knee extensors, the abdominal and spinal muscles and, unless unimpaired as compared with the ankle dorsiflexors, the calf muscles; also the abductors of the humerus, the wrist flexors and the muscles which bring the thumb out from the palm to face the other fingers. No massage or manipulation should be allowed during the sensitive stage.[12p] Even if the bladder is completely paralyzed, catheterization should not be done; the bladder will eventully empty itself reflexly.

Treatment with Serum.—The serum of convalescent patients and of 80 per cent of adults neutralize the poliomyelitis virus,[77] but when either

76. Landon and Smith.[1] Caverly and others.[12m] MacAusland.[12n] Footnote 12*p*. Ruhräh.[12r] Turslow, W.: M. J. & Rec. **135**:31, 1932. Ruhräh, J.: Treatment of Poliomyelitis: Prevention of Deformity and Protection of Muscles, J. A. M. A. **100**:1587 (May 20) 1933. Jones, E. A.: New England J. Med. **209**:831, 1933. Gaenslen, F. J.: Aids in Muscle Training, with Special Reference to Sling Suspension and Underwater Exercises, J. A. M. A. **104**:1002 (March 23) 1935.

77. (*a*) Kramer.[15f] (*b*) Footnote 27. (*c*) Flexner, S., and Lewis, P. A.: Experimental Poliomyelitis in Monkeys, J. A. M. A. **54**:1780 (May 28) 1910. (*d*) Netter, A., and Levaditi, C.: Compt. rend. Soc. de biol. **68**:617, 1910. (*e*) Toomey.[52b] (*f*) Howitt, B. F.: J. Infect. Dis. **51**:565, 1932. (*g*) Hudson, N. P., and Litterer, W.: ibid. **53**:304, 1933. (*h*) Southby, R., and McKie, M.: M. J. Australia **2**:404, 1933. (*i*) Brodie, M.: J. Exper. Med. **56**:493 and 507, 1932; Science **79**:594, 1934; Proc. Soc. Exper. Biol. & Med. **32**:300, 1934; New York Times, Nov. 5, 1935, p. 10. (*j*) Brodie, M., and Park, W. H.: Active Immunization in Poliomyelitis, Am. J. Dis. Child. **50**:537 (Aug.) 1935; Active Immunization Against Poliomyelitis, J. A. M. A. **105**:1089 (Oct. 5) 1935; Am. J. Pub. Health **26**:119, 1936. Netter, A.; Gendron, and Touraine: Compt. rend. Soc. de biol. **70**:625, 707 and 739, 1911. Levinson, S. O.; McDougal, C., and Thalhimer, W.: Acute Anterior Poliomyelitis in the Chicago Area in 1931, J. A. M. A. **99**: 1058 (Sept. 24) 1932. Gerstley, J. R.: M. Clin. North America **16**:517, 1932. Richardson, D. L., and West, E. J.: Rhode Island M. J. **15**:100, 1932. Schottmüller, E.: Deutsche med. Wchnschr. **59**:43, 1933. Daneri: Rev. chilena de pediat. **4**:449, 1933. Sherman, I.: Acute Poliomyelitis, Am. J. Dis. Child. **47**:532 (March) 1934. Sands, J. J.: J. Nerv. & Ment. Dis. **75**:601, 1932; New York State J. Med. **34**:587, 1934. Siegl, J.: Wien. klin. Wchnschr. **47**:237, 1934. Török, G.: Med. Klin. **30**:1093, 1934.

of these serums is administered intraspinally it probably does more harm than good.[1] Many still believe that serum has value when given intravenously or intramuscularly as soon as the first symptoms occur and before the onset of paralysis,[78] especially in large amounts from 100 to 300 cc.[79] and by transfusion. However, the evidence gained by treating alternate patients and by the observation of controls seems to show conclusively that no benefit is produced.[80] In a small series of cases in which two or more large intravenous transfusions were given, no improvement could be demonstrated. No deaths occurred, but several of the patients had severe reactions.[2f] Deaths have followed the injection of human serum.[81] An excellent study of the pros and cons of this question has recently been published.[1]

Horses,[82] goats,[83] sheep,[83] monkeys [5b] and rabbits have been inoculated repeatedly with poliomyelitis virus, and as the neutralizing power of the serum increased it has been used therapeutically, but apparently without clinical benefit.[84] An antipoliomyelitis streptococcus serum is

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78. Henry and Johnson.[2d] Footnote 12*p*. Schultz.[15e] Taillens.[20b] London and Roberts.[44b]

79. Footnote 58*i*. Brown.[58j]

80. (*a*) Landon and Smith.[1] (*b*) Footnote 2*m*. (*c*) Kramer.[18g] (*d*) Landon.[51] (*e*) Baastrup.[55a] (*f*) Round Table Discussion on Poliomyelitis, J. Pediat. **7**:277, 1935. (*g*) Kramer, S. D.; Aycock, W. L.; Solomon, C. I., and Thenebe, C. L.: New England J. Med. **206**:432, 1932. (*h*) Kramer, S. D.: Am. J. Pub. Health **22**:380, 1932. (*i*) Report of a Study of Administration of Convalescent Serum in the Treatment of Poliomyelitis, Bull. New York Acad. Med. **8**:613, 1932. (*j*) Park, W. H.: Therapeutic Use of Antipoliomyelitis Serum in Preparalytic Cases of Poliomyelitis, J. A. M A. **99**:1050 (Sept. 24) 1932. (*k*) Hudson, N. P., and Lennette, E. H.: J. Prev. Med. **6**:335, 1932. (*l*) Previtali, G.: Arch. Pediat. **49**:540, 1932. (*m*) Wesselhoeft, C.: J. Pediat. **3**:330, 1933. (*n*) Hoeffler, H.: München. med. Wchnschr. **80**:1367, 1933. (*o*) Harmon, P. H.: Poliomyelitis: Experimental and Theoretical Basis for Serum Therapy; Review, Am. J. Dis. Child. **47**:1179 (June) 1934. (*p*) Fischer, A. E.: Human Convalescent Serum in Treatment of Preparalytic Poliomyelitis: Comparison of 447 Treated and 102 Control Patients in New York City in 1931, ibid. **48**:481 (Sept.) 1934. (*q*) Schultz, E. W., and Gebhardt, L. P.: J. Pediat. **6**:615, 1935. (*r*) Brodie, M.: J. Immunol. **28**:353, 1935. (*s*) Park, W. H., and Brodie, M.: Active Immunization Against Poliomyelitis, Am. J. Dis. Child. **50**:1077 (Oct.) 1935.

81. Sudden Death After the Injection of Human Serum, current comment, J. A. M. A. **103**:192 (July 21) 1934.

82. Pettit, A.: Compt. rend. Soc. de biol. **81**:1087, 1918. Fairbrother, R. W., and Morgan, W. T. J.; Brit. J. Exper. Path. **11**:298, 1930. Weyer, E. R.; Park, W. H., and Banzhaf, E. J.: J. Exper. Med. **53**:553, 1931.

83. Howitt, B. F.; Shaw, E. B.; Thelander, H. E., and Limper, M.: Immunization of Goats and Sheep to Poliomyelitis Virus: Clinical Application of Their Serums, J. A. M. A. **96**:1280 (April 18) 1931. Howitt, B. F.: J. Infect. Dis. **50**:26 and 47, 1932. Orel, H.: Wien. klin. Wchnschr. **46**:590, 1933.

84. Landon and Smith.[1] Schultz.[15e]

available but not recommended.[85] Normal horse serum, diphtheria antitoxin and antimeningococcus and pneumococcus serums administered intranspinally apparently have no value.[86] Autotherapy with the patient's spinal fluid and blood is useless.[1]

Other Methods.—Repeated lumbar punctures and continued spinal drainage while "forcing" hypotonic saline solutions,[87] intravenous administration of hypertonic solutions to reduce cerebral edema,[88] irritation therapy, e. g., intramuscular injections of milk [89] and intraspinal administration of methenamine,[90] roentgen therapy,[91] fever therapy,[92] and injections of a solution of manganese butyrate [93] have been advocated, but the number of patients treated by these methods is too small for conclusions to be drawn.

Respirators occasionally save lives, but selection of the type of patient who will be benefited by a respirator requires considerable experience and judgment.[94] In New York in 1931 nearly five times as

85. Nuzum, J. W., and Willy, R. G.: Specific Serum Therapy of Epidemic Poliomyelitis, J. A. M. A. **69**:1247 (Oct. 13) 1917. Amoss, H. L., and Eberson, F.: J. Exper. Med. **27**:309, 1918. Rosenow, E. C.: Poliomyelitis Antistreptococcus Serum, J. A. M. A. **94**:777 (March 15) 1930. Clarke, F. S.: Nebraska M. J. **17**:283, 1932.

86. Landon and Smith.[1] Baastrup.[8b]

87. Retan, G. M., and Kubie, L. S.: Bull. Neurol. Inst. New York **1**:419, 1931. Retan, G. M.: Forced Spinal Drainage in Its Relation to Infections of the Central Nervous System, J. A. M. A. **99**:826 (Sept. 3) 1932; The Development of the Therapeutic Use of Forced Perivascular (Spinal) Drainage, ibid. **105**:1333 (Oct. 26) 1935.

88. Caverly and others.[12m] Weed, L. H.: J. M. Research **26**:93, 1914-1915. Aycock, W. L., and Amoss, H. L.: The Treatment of Acute Poliomyelitis, J. A. M. A. **81**:474 (Aug. 11) 1923. Smith, T. C.: Intravenous Injection of Hypertonic Salt Solution in Acute Poliomyelitis, Am. J. Dis. Child. **31**:360 (March) 1926. Neal,[12] chap. 5.

89 (*a*) Thenebe and Cenci.[2h] (*b*) Finck, H.: München. med. Wchnschr. **79**:1843, 1932. (*c*) Barla-Szabó, E.: Wien. klin. Wchnschr. **48**:81, 1935.

90. Teysel, O.: Časop. lék. česk. **70**:1796, 1931.

91. Landon and Smith.[1] Gentili.[18k] Finck.[89b] Barla-Szabó.[89c] Bordier, H., and Gonjon, A.: Paris méd. **1**:564, 1932. Gracoski, S.: Bull. Soc. de pediat. de Iasi **3**:122, 1932. Kadrnka, G.: Arch. d'électric. méd. **41**:167, 1933.

92. Krause.[29] Jungeblut, C. W., and Kopeloff, N.: J. Infect. Dis. **49**:348, 1931.

93. Barge, A. A.: J. M. A. Georgia **23**:319, 1934.

94. (*a*) Landon and Smith.[1] (*b*) Brahdy and Lenarsky.[59c] (*c*) Shaw and others.[59d] (*d*) Wilson.[59e] (*e*) Wesselhoeft, C., and Smith, E. C.: New England J. Med. **207**:560, 1932. (*f*) Wilson, J. L.: Respiratory Failure in Poliomyelitis: Treatment with Drinker Respirator, Am. J. Dis. Child. **43**:1433 (June) 1932. (*g*) Harper, P., and Tennant, R., Jr.: Yale J. Biol. & Med. **6**:31, 1933. (*h*) Smith, E.: Respiratory Failure and the Drinker Respirator in Poliomyelitis, J. A. M. A. **100**:1666 (May 27) 1933. (*i*) Crone, N. L.: New England J. Med. **210**:621, 1934.

many patients treated in a respirator died as compared with those not so treated.[95] The harm produced by alveolar emphysema, which has been observed at some autopsies, may outweigh the benefit.

Treatment of the Bulbar Type of Polioencephalitis.—The foot of the bed should be elevated, for postural drainage; mucus and other secretions should be aspirated by suction from the throat and larynx; sufficient sedatives should be given to keep the patient quiet (although the risk of pneumonia should be remembered); liquid food should be administered in small amounts (by nasal tube if swallowing is impossible);[54] fluids should be given parenterally or through the rectum; oxygen and carbon dioxide may be necessary for cyanosis, and, last but not least, a respirator should not be used, as it probably does more harm than good in cases of the bulbar type.[96] Drugs (ephedrine, atropine, etc.) and lumbar puncture are not recommended.[97] A tracheotomy may be necessary.

After-Care of Persons with Paralysis.—Advances in this field, started by Taylor in 1867,[12d] have equaled, if not surpassed, the progress in etiologic studies. The hopeless cripple of the last generation is rarely seen today. A complete examination of the muscles should be made as soon as the sensitiveness is over.[12p] When recuperation is well established, carefully supervised gentle exercise, particularly voluntary movements within the capacity of the muscle, is of value. Warm salt baths, very gentle massage (after all tenderness has disappeared), fresh air, sunlight and warmth are beneficial.[12r] Training of the muscles should be done only by some one who has a thorough knowledge of functional anatomy; it should be preceded by baking and massage to increase the circulation in the part and should be increased gradually.[12p] Fatigue must be avoided.[12p]

The transition to weight bearing should not be allowed as long as recovery is expected; then it should be gradual, and overexertion and fatigue should be avoided.[12r] When the patient with weakened legs or trunk is standing, splints should be applied to hold the feet and knees in their normal position, and a corset or jacket should be used to hold the trunk in its normal position, to prevent deformity.[98] These should be inspected frequently and changed as necessary.[12r] Swimming does not take the place of localized training of muscles and may cause harmful contractions in the muscles which oppose the weaker, paralyzed ones. Treatment in water has no more specific value than treatment

95. Landon and Smith.[1] Landon.[51]

96. Brahdy and Lenarsky.[59e] Shaw and others.[59d] Wesselhoeft and Smith.[94e] Wilson.[94f] Harper and Tennant.[94g] Smith.[94h] Crone.[94i]

97. Landon.[51] Smith, E., and Fineberg, H. L.: J. Pediat. **4**:590, 1934.

98. Underwood.[3] Footnote 12*p*.

on a table, but it is a pleasant way of doing exercises. The buoyancy of the water allows weak muscles to perform their function more easily than is possible otherwise.[12p] Injection of a solution of ephedrine and lumbar ganglionectomy have been used to increase the supply of blood to the paralyzed part to prevent wasting.[99] Surgical procedures, such as the transposition of tendons, should be deferred until at least two years after the acute stage. Mechanical braces and instruction in their use have enabled many severely paralyzed patients who otherwise would be bedridden to maintain an active life.

PREVENTION

Active Immunization.—The brains and spinal cords of monkeys infected with the poliomyelitis virus have been suspended in solution of formaldehyde to make a vaccine of killed virus (the method of Brodie and Park[100]) and with sodium ricinoleate to make a vaccine of live virus (the method of Kolmer[101]), and these vaccines have been injected into more than 10,000 children. Some of these children had abscesses or fever,[101] and paralysis was observed in 12, of whom 6 were reported as having died.[102] It may still be too early to conclude whether death was due to infection with the vaccine, whether the vaccine was given during the incubation period of poliomyelitis or whether any of those vaccinated were actively immunized.[103] However, it has been suggested that the vaccine of killed virus may not immunize and that there is a risk with the vaccine of live virus.[104] Further drawbacks

99. Telford, E. D., and Stopford, J. S. B.: Brit. M. J. **2**:770, 1933. Herzfeld, G.: Edinburgh M. J. **40**:172, 1933. Robertson, D. E.: Surg., Gynec. & Obst. **58**:212, 1934. Royle, N. D.: M. J. Australia **1**:486, 1935.

100. Park and Brodie.[80s] Brodie.[77i] Brodie and Park.[77j]

101. Kolmer, J. A., and Rule, A. M.: J. Immunol. **26**:505, 1934; Am. J. M. Sc. **188**:510, 1934. Kolmer, J. A.; Klugh, G. F., Jr., and Rule, A. M.: A Successful Method for Vaccination Against Acute Anterior Poliomyelitis, J. A. M. A. **104**:456 (Feb. 9) 1935. Kolmer, J. A.: Susceptibility and Immunity in Relation to Vaccination in Acute Anterior Poliomyelitis, ibid. **105**:1956 (Dec. 14) 1935; Am. J. Pub. Health **26**:126 and 148, 1936. Johnson, W. M.: South. Med. & Surg. **97**:570, 1935.

102. Leake, J. P.: Poliomyelitis Following Vaccination Against This Disease, J. A. M. A. **105**:2152 (Nov. 26) 1935.

103. (*a*) Schultz and Gebhardt.[15h] (*b*) Footnote 80*f*. (*c*) Flexner S.: Science **82**:420, 1935. (*d*) Infantile Paralysis Vaccines, current comment, J. A. M. A. **105**:1275 (Oct. 19) 1935. (*e*) Rivers, T. M.: Am. J. Pub. Health **26**:136, 1936. (*f*) Discussion of Poliomyelitis Papers, Am. J. Pub. Health **26**:143, 1936.

104. Schultz.[15e] Schultz and Gebhardt.[15h] Flexner and Lewis.[77c] Netter and Levaditi.[77d] Footnote 80*f*. Flexner.[103c] Footnote 103*d*. Rivers.[103e] Footnote 103*f*.

are that injection of brain tissue may cause demyelinization [105] and that a reaction may take place similar to that which occurs in approximately 1 of every 3,528 persons after injections of spinal cord in the Pasteur antirabic treatment and which is sometimes fatal.[106]

Nonspecific Active Immunity.—It has been reported that the serum of monkeys immunized with diphtheria toxin-antitoxin and toxoid neutralizes the poliomyelitis virus.[107] On the other hand, in one series 16 of 18 patients had a negative Schick reaction, indicating that immunity to diphtheria did not protect against poliomyelitis.[2f] Prophylaxis with placental extract, similar to that against measles,[108] has been suggested. The treatment of the nasal mucosa with alum [109] or ultraviolet ray [110] may prevent the entrance of the virus.

Passive Immunization.—Because of their neutralizing power,[111] some believe that injections or transfusions of convalescent or adult serum or blood protect against poliomyelitis or make the attack less severe,[112] but the evidence seems to be to the contrary.[113]

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105. Rivers, T. M.; Sprunt, D. H., and Berry, G. P.: J. Exper. Med. **58**:39, 1933. Schwentker, F. F., and Rivers, T. M.: ibid. **60**:559, 1934; Experimental Production in Monkeys of an Encephalomyelitis Accompanied by Myelin Destruction, Am. J. Dis. Child. **50**:536 (Aug.) 1935. Rivers, T. M., and Schwentker, F. F.: J. Exper. Med. **61**:689, 1935.

106. Horack, H. M.: Reaction to Pasteur Treatment, to be published.

107. Footnote 27. Jungeblut.[31b]

108. McKhann, C. F., and Chu, F. T.: Use of Placental Extract in Prevention and Modification of Measles, Am. J. Dis. Child. **45**:475 (March) 1933.

109. Armstrong, C., and Harrison, W. T.: Pub. Health Rep. **50**:725, 1935. Gordon, F. B.; Harrison, J. A., and Hudson, N. P.: Proc. Soc. Exper. Biol. & Med. **32**:689, 1935.

110. Peskind, S.: Protection Against Poliomyelitis Through Blockade of Olfactory Tracts or Bulbs of Their Terminal Fibers, J. A. M. A. **106**:483 (Feb. 8) 1936.

111. Kramer.[15f] Paul and Trask.[15g] Footnote 27. Flexner and Lewis.[77c] Netter and Levaditi.[77d] Toomey.[52b] Howitt.[77f] Hudson and Litterer.[77g] Southby and McKie.[77h]

112. (*a*) Toomey.[52b] (*b*) Rohmer, W. G., and Wallgren, B.: Bull. Assoc. internat. de pédiat. prevent. **1**:12, 1933. (*c*) Stokes, J., Jr.; Wolman, I. J.; Carpenter, H. C., and Margolis, J.: Prophylactic Use of Parents' Whole Blood in Anterior Poliomyelitis, Am. J. Dis. Child. **50**:581 (Sept.) 1935.

113. Henry and Johnson.[2d] Footnote 2*m*. Footnote 12*p*. Schultz and Gebhardt.[15h] Waltner.[18h] Kissel and others.[60f] Carpenter, H. C.; Stokes, J., Jr., and Wolman, I. J.: The Evaluation of Parents' Whole Blood as a Prophylactic Measure in Anterior Poliomyelitis, Am. J. Dis. Child. **46**:681 (Sept.) 1933. Stokes and others.[112c] Schultz, E. W., and Gebhardt, L. P.: J. Pediat. **6**:615, 1935; **7**:332, 1935.

Acquired Immunity.—Since only 18 instances of a second attack of poliomyelitis and only 1 of a third attack have been reported,[114] and since the incidence in adults and in city dwellers [115] is so much lower than that in children and in the rural population, immunity is probably acquired from either definite or subclinical infection. An analogous observation is the rarity of summer epidemics in areas in which sporadic cases were frequent during the preceding winter.[10] The gradual development of immunity with age (maturation), which has been suggested,[116] has not been proved.

Quarantine and Isolation.—Isolation for three weeks of patients and those who had been in contact with them has been required by many boards of health since 1916, but the evidence then and now does not indicate that anything is accomplished by this procedure.[117] If the disease is spread by contact and droplet infection from the rhinopharynx,[118] why are the paralytic manifestations not prevalent in the winter, as are colds and other diseases caused by droplet infection?[18o] Insects and dust seem exonerated as means of transmission,[119] but some epidemics apparently have been traced to water [15a] and milk.[1] Granted, however, that poliomyelitis is spread by nasal droplets, who should be quarantined? The disease rarely attacks more than 1 member of a family, and cases in which the disease develops from contact are conspicuously rare.[120] Of 2,070 persons exposed, only 14 contracted the disease.[18o] In North Carolina in 1935 only 8 patients of 622 had a history of contact with another patient.[15d] Carriers and patients with the nonparalytic or subclinical type of the disease must be so common [121] that nearly the whole population should be isolated. Obviously, physicians and hospital personnel should protect themselves by masks, hand washing, nasal sprays of alum,[109] etc.,[1] because of the higher incidence of poliomyelitis among

114. Quigley, T. B.: Second Attacks of Poliomyelitis, J. A. M. A. **102**:752 (March 10) 1934. Moore, T.: Brit. M. J. **2**:166, 1934. Tesdal, M.: Norsk mag. f. lægevidensk. **95**:978, 1934. Cohen, L.: New England J. Med. **213**:601, 1935.

115. Ullrich.[15e] Root.[15d] Schultz.[15e] Kramer.[15f] Paul and Trask.[15g] Schultz and Gebhardt.[15h]

116. Jungeblut and Engle.[18r] Friedberger, E.; Bock, G., and Furstenheim, A.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **64**:294, 1929.

117. Baastrup.[8b] Footnote 12*i*.

118. Landon and Smith.[1] Wickman.[2b]

119. Landon and Smith.[1] Footnote 12*o*. Rankin.[18o]

120. (*a*) Landon and Smith.[1] (*b*) Henry and Johnson.[2d] (*c*) Satos and Rubin.[2e] (*d*) Root.[15d] (*e*) Peck.[18l] (*f*) Stewart, W. B.: J. Pediat. **2**:393, 1933.

121. Paul, J. R.; Trask, J. D., and Webster, L. T.: J. Exper. Med. **62**:245, 1935.

them.[122] But are the usual regulations and the hysteria that they cause worth while?

Before prevention can be placed on the same basis as that of diphtheria, a simple test for detecting susceptible persons is needed.[15h] At present, determination of the neutralizing power of the serum, which is expensive and time-consuming, is the only method; colloidal gold, complement fixation, precipitin and skin tests are useless.[43]

CONCLUSION

The sum of the present knowledge seems to be that poliomyelitis is an infectious disease of the nervous system due to a virus, which sometimes causes paralysis, and that, except for rest in bed, protection of weak muscles during the acute stage and orthopedic treatment of the after-effects, adequate therapy and prevention are still in the future.

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122. Kissel and others.[60f] Stewart.[120f]

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following twenty-four physicians have been certified by the American Board of Pediatrics since the last report:

Harry S. Altman, New York; Louis Barash, New York; Walter Douglas Brown, Beaumont, Tex.; Fred W. Bush, Rochester, N. Y.; Nicholas Boddie Cannady, Dothan, Ala.; Charles Rowse Dengler, Jackson, Mich.; R. Bruce Eldredge, Omaha; Edward Porter Essertier, Hackensack, N. J.; George Julius Feldstein, Pittsburgh; Alfred Elias Fischer, New York; Edward O. Fitch, Houston, Tex.; James LeRoy Foster, Pittsburgh; Hugh C. Graham, Tulsa, Okla.; Theodore P. Herrick, Cleveland; George Russell Irving, New York; Sidney David Kramer, Brooklyn; Alfred Gustav Langmann, New York; George P. Laton, Los Angeles; Mathilde Loth, New York; Mary Schwartz Newman, Brooklyn; Maurice J. Searle, Tulsa, Okla.; Harry M. Shapiro, New York; Edwin August Socola, New Orleans, and Edwin B. Weldon, Bridgeport, Conn.

None of these were examined.

A New Magazine.—"Medical Classics," is being published by the Williams & Wilkins Company. This will fill a want which is much felt and will recall the accomplishments of former members of the medical profession, which will probably make physicians of the present day more humble in estimating the value of their own achievements.

SOCIETY NEWS

The Congrés International et Congrés National des Colonies de Vacances et Oeuvres de Plein Air will meet in Paris, from July 1 to 4, 1937.

The fourteenth annual meeting of the American Orthopsychiatric Association will be held at the Roosevelt Hotel in New York from Feb. 18 to 20, 1937. The president of the society is Dr. Edgar A. Doll. The secretary is Dr. George S. Stevenson, 50 West 50th Street, New York.

Obituaries

W. McKIM MARRIOTT, M.D.

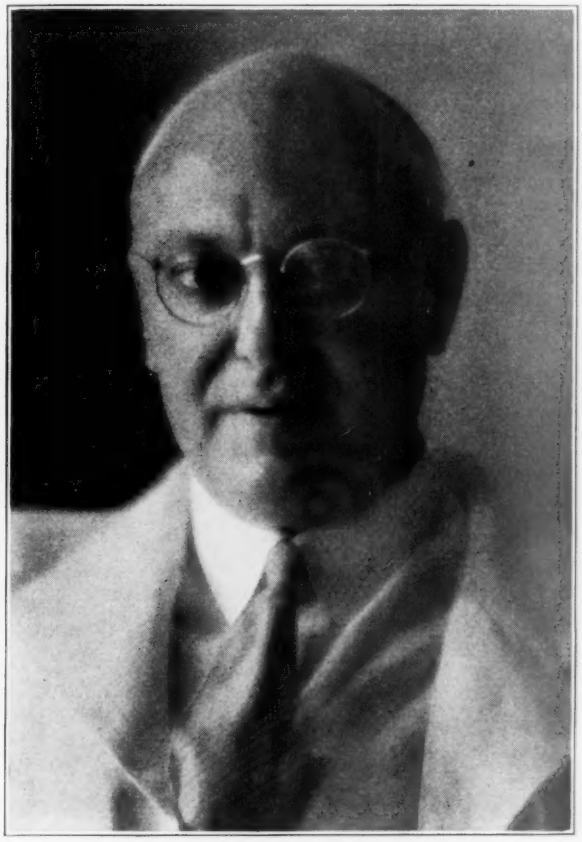
1885-1936

Dr. Marriott died on November 11 of complications resulting from appendicitis. He was 51 years old, at the peak of productiveness, with a remarkably brilliant career behind him and with every reason to expect a decade or two more of active life.

One may, of course, but speculate desolately on what the future might have held for him had he not gone to this most premature and untimely end. In sorrow at his passing one should, however, be greatly comforted in reviewing what he had accomplished. Early in life he indicated his love of chemistry. Because of his unusual interest in and ability to understand this subject, he was given a student assistantship in chemistry at the University of North Carolina for three years before his graduation, which occurred in 1904. His exceptional ability to teach and to conduct research in chemistry won for him an assistantship in biochemistry at Cornell University, where he obtained his degree in medicine in 1910. He then went to Washington University, St. Louis, to work four years with Prof. P. A. Shaffer in biochemistry. At this time he became greatly interested in medicine. Although he really wished to study medicine as an internist, his opportunity came when the late Dr. John Howland, of Johns Hopkins University, with his customary keen perception, realized Dr. Marriott's capabilities and undertook to be his clinical teacher in pediatrics. It was probably most fortunate that circumstances directed him into the field of pediatrics, because of the unusual opportunity in this field for applying biochemical knowledge to the study and treatment of diseases.

In 1917 he was made professor of pediatrics at Washington University and physician in chief of the St. Louis Children's Hospital. If there was doubt or misgiving in the mind of any one as to the wisdom of appointing so young a man (for he was then only 32 years old) to fill these positions, it must soon have been completely dispelled by the rapid succession of brilliant researches in the field of infant nutrition which soon followed and which proved to be the groundwork for the later much needed simplification of the artificial feeding of infants. This pioneer work, which included the development of methods for the determination of serum calcium and carbon dioxide tension, not only led to fundamental knowledge of the pathogenesis of infantile

rickets and tetany but also increased immensely the understanding of changes occurring in the body as the result of sudden and extensive losses of water and mineral salts and deprivation of food. In the April 1923 number of *Physiological Reviews* he published a masterful monograph on "anhydremia" (a word which he coined), which explained to what a great extent the symptoms of acute intestinal intoxication and



W. McKIM MARRIOTT, M.D.
1885-1936

shock are due to the reduction of the volume and flow of the blood which results from loss of plasma water. Then followed notable clinical and scientific investigations on the effect of acute and chronic infections in infants and children, which added much to the understanding of the enteral and parenteral causes of diarrhea and the mode of production of malnutrition. It was Dr. Marriott who first recommended frequent intravenous infusion of dextrose and insulin as a treatment of mal-

nutrition for infants and children who could not digest or assimilate sufficient food to meet their caloric needs, and perhaps the very last of his clinical interests was centered on another abnormality of carbohydrate metabolism, hypoglycemia.

In addition to the time and effort expended in actual research, Dr. Marriott constantly gave of himself further in making the fruits of his study generally available by his extensive undergraduate and postgraduate teaching, lectures and frequent association with his professional colleagues at medical meetings, with the result that his identity and work became as well known in the far corners of the world as in the university where he worked and was dean from 1923 to 1936. On July 1, 1936, Dr. Marriott relinquished his position as dean and as professor of pediatrics of the Washington University School of Medicine and as physician in chief of the St. Louis Children's Hospital to become dean and director of research at the University of California School of Medicine. It was shortly after this move that this truly great man was struck down by the hand of death.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

Duration of Demonstrable Antibodies in the Serum of Rabbits Immunized with Heat-Killed Type II and Type III Pneumococci. Ernest G. Stillman, J. Infect. Dis. **57**:223 (Nov.-Dec.) 1935.

The author's conclusions are as follows:

"Development of type specific agglutinins and protective antibodies bear little or no relation to the amounts of antigen administered.

"Comparative analysis shows that type specific agglutinins persist for relatively short periods in the circulating blood.

"Type specific protective antibodies persist longest following immunization with type I pneumococci, disappear sooner following injections of type II organisms, and last but a short period following treatment with type III antigen.

"Antibody response does not appear to bear any relation to the virulence of the culture used as antigen."

Toomey, Cleveland.

The Reaction of Partially Immunized Rabbits to Inhalation of Type I Pneumococci. Ernest G. Stillman and R. Z. Schulz, J. Infect. Dis. **57**: 233 (Nov.-Dec.) 1935.

The authors' conclusions are as follows:

"Following inhalation of virulent pneumococci, partially immunized rabbits failed to show any evidence of pulmonary localization of the infection.

"An increased resistance to virulent pneumococci may be established in rabbits by a single injection of a small amount of antigen.

"Alcohol intoxication of partially immunized rabbits did not materially alter the mortality or pulmonary reactions following infection by inhalation."

Toomey, Cleveland.

The Reaction of Normal and Partially Immunized Rabbits to Intranasal Instillation of Type I Pneumococci. Ernest G. Stillman and R. Z. Schulz, J. Infect. Dis. **57**:238 (Nov.-Dec.) 1935.

The authors' conclusions are as follows:

"Rabbits may be more regularly infected by intranasal instillation than by inhalation of pneumococci.

"The mortality of rabbits so infected varies in direct proportion to the number of pneumococci that are instilled into the nose.

"A single intoxicating dose of alcohol does not materially alter the mortality of rabbits following intranasal instillation.

"Following intranasal inoculation, the perivascular lymphatics may be characteristically involved. The dilatation of the lumen of the lymphatics, and the infiltration of the surrounding interstitial tissue by leucocytes, often formed a definite collar about the larger vessels. In the more advanced cases, the walls of the vessels themselves are infiltrated by leucocytes, and vascular thrombi are finally formed.

"Under the condition of these experiments, lobar pneumonia could not be produced."

Toomey, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

CALCIUM AND PHOSPHORUS NEEDS OF PRESCHOOL CHILDREN. AMY L. DANIELS, MARY K. HUTTON, E. M. KNOTT, OLIVE E. WRIGHT and MARY FORMAN, J. Nutrition **10**:373 (Oct.) 1935.

Earlier work by the same authors had indicated that the average retention of calcium might be the same whether the child was receiving 1 pint or 1 quart (473.2 or 946.4 cc.) of milk per day. These findings were in disagreement with previously established figures by other workers which indicated that 1 quart of milk daily is necessary to supply the calcium for children of the ages considered.

The present work was done among a group of healthy children aged between 36 and 66 months. Important influencing factors were carefully controlled, and all the children received an adequate amount of vitamin D. The results as revealed in this experiment verify the former conclusions and indicate that from 45 to 50 mg. of calcium per kilogram of body weight is sufficient for the age group studied, provided the calcium is available and sufficient vitamin D is allowed.

The need for phosphorus seems to be about from 55 to 60 mg. per kilogram of body weight. Adequate vitamin D is required in this case also.

The retention of calcium and that of phosphorus—between 7 and 9 mg. and between 6 and 10 mg., respectively, per kilogram of body weight—seem normal for well developed children of the age group studied. MUNNS, Winnetka, Ill.

HUMAN IODINE BALANCE. VERSA V. COLE and GEORGE M. CURTIS, J. Nutrition **10**:493 (Nov.) 1935.

Comparatively little investigation of the iodine balance in human beings has been done. The authors succeeded in determining several interesting facts after varying periods of study on five persons. They observed that the combined iodine content of the urine and the stool may account for less than 50 per cent of the intake of iodine and that there was a fairly uniform output of iodine for a person on a monotonous diet. In two subjects studied, previous observations by Scheffer of an increased amount of fecal iodine in hyperthyroidism were confirmed. MUNNS, Winnetka, Ill.

AUTO-REGULATION OF THE METABOLISM. S. LEITES, Ann. de physiol. **11**:125, 1935.

Studies of blood fat were made on man and on the dog. Blood fat is to a certain degree independent of the quantity of neutral fat ingested. There is normally a threshold of neutral fats of the blood which is generally not passed. The reaction of the blood fat and acetone to the ingestion of fat is determined especially by the initial figures for neutral fat and acetone bodies of the blood in a state of fasting. The neutral fat of the blood during fasting is relatively low—60 mg. per hundred cubic centimeters. Ingestion of fat causes hyperlipemia and hyperacetonemia, which, after from six to nine hours, is followed by a hypolipemic and hypo-acetonemic phase. If the neutral fat during fasting is above from 60 to 90 mg. the ingestion of butter causes hypolipemia and hypo-acetonemia.

The respiratory quotient reacts in the same way to the ingestion of fat. If the quotient is low, up to 85, it rises after the ingestion of fat (butter), but if it is above 88 the ingestion of fat lowers it. In other words, when it is principally the fats that are burning in the organism, the exogenous introduction of fat diminishes their combustion. If, on the contrary, it is the carbohydrates which are burning, the exogenous introduction of fat is followed by the combustion of fat. Fat, then, is itself a powerful regulator of the metabolism of fats.

Leites defines the fat and acetone threshold as the minimal quantity of neutral fat and of acetone body in the blood of a fasting animal which suffices for the ingestion of fat to be able to provoke hypolipemia and hypo-acetonemia. For

healthy subjects the threshold for fat is between 60 and 90 mg. per hundred cubic centimeters, and the threshold for acetone, between 6 and 9 mg.

In diabetes the threshold for fat and for acetone is elevated, the degree of elevation being proportional to the severity of the disease. Insulin causes a fall in the threshold.

In obesity the threshold for fat is lowered. There appears to be a lipophilic condition of the tissues as the result of the inability to eliminate and mobilize fats by autoregulation.

The authors have proved the existence of analogous phenomena in the autoregulation of the nitrogen metabolism. The introduction of peptone or of amino-acid when there is a high nitrogen content of the blood, due to previous injection of peptone, is not followed by a new elevation of the nitrogen content of the blood but causes a phase in which the nitrogen level is lowered.

The mechanism by which fat and nitrogen are regulated would appear to be divided into two steps. The first, which is ontogenetically and phylogenetically the older, is evidently the direct regulatory action of the chemical substances involved in the fat and the nitrogen metabolism, exercised on the diverse phases of the corresponding metabolism. The other step, which belongs to an epoch ontogenetically and phylogenetically less distant, must manifest itself by adequate stimulation of the endocrine glands and of vegetative centers.

BUDSON, Detroit.

METABOLISM OF INORGANIC SUBSTANCES IN THE LIVER OF THE CALF IN THE COURSE OF FETAL DEVELOPMENT: I. IRON, PHOSPHORUS and CALCIUM. Z. GRUZEWSKA and M. G. ROUSSEL, Ann. de physiol. **11**:176, 1935.

The liver of the fetal calf contains a minimal amount of iron during the first six to seven months. At eight and one-half to nine months the amount of iron increases rapidly. These high values for iron at the end of pregnancy seem to confirm the original hypothesis of Bunge of an iron reserve stored in the fetal liver just before birth.

The total amount of phosphorus in the fetal liver decreases regularly during intra-uterine life. At the time of the formation of the extremities and of ossification the authors found 0.903 Gm. of phosphorus per hundred grams of fresh tissue, a value which corresponds to 3 Gm. of phosphoric acid. One can consider this high value for phosphorus as a true reserve for growth and ossification of the embryo.

The inorganic compounds of phosphorus increase during fetal development at the expense of the organic fractions of phosphorus. It would appear that the phosphates accumulated in the fetal liver at the beginning of development are for the most part composed of organic phosphates.

The calcium shows only slight variations in value in the course of fetal development. However, one can note at about from four to eight months a mild increase of this inorganic element in the liver. BUDSON, Detroit.

SWEETENED CONDENSED MILK IN THE NUTRITION OF SICK AND WELL INFANTS. J. TAILLENS, Arch. de méd. d. enf. **38**:737 (Dec.) 1935.

Taillens has used sweetened evaporated milk exclusively in his clinic at the University of Lausanne for more than twenty years. The mixture that he recommends consists of whole milk, the coefficient of concentration being 2.6. To this is added 16 Kg. of cane sugar for each 100 Kg. of fresh milk, the entire percentage of solids being 32.5.

With this preparation the author has secured results far more satisfactory than with any other not only among infants suffering from various types of dyspepsia with regurgitation, vomiting and resulting atrophy, but also among those in the clinic for well babies. Historical data are reviewed, and many observations in support of this regimen are reported. AMESSE, Denver.

RELATION BETWEEN THE ALKALI RESERVE OF BLOOD PLASMA AND THAT OF CEREBROSPINAL FLUID IN CHILDREN DURING HEALTH AND DISEASE. STEFANO MOSCHINI, Pediatria **43**:407 (April) 1935.

This study was undertaken with a view of establishing the relation of the alkali reserve of the blood plasma and that of the cerebrospinal fluid in health and illness. The series studied was made up of fourteen children from 2 to 9 years of age who were clinically and physically normal and of nineteen children from 1 to 9 years of age who had the following diseases in active forms: acute nephritis, typhoid, dysentery, pneumonia and pneumonia complicated by meningitis.

Moschini summarizes his conclusions as follows:

In normal children the alkali reserve of the blood is superior to that of the cerebrospinal fluid, the average being 56 volumes per cent of carbon dioxide for the blood and 50.7 volumes per cent for the spinal fluid. The average difference between the two is 9 per cent. In the normal children the alkali reserve in the spinal fluid is more constant and presents lesser oscillations than that in the blood plasma. In nephritis the alkali reserve of the spinal fluid does not exhibit a decrease parallel to that of the alkali reserve in the blood plasma, which during the active phases of the disease falls lower than that of the spinal fluid.

In certain stages of meningitis, in which there is a sudden fall of the alkali reserve of the cerebrospinal fluid, the lowering of the alkali reserve of the blood plasma is only slight. (The average difference between the two is then near 23 per cent instead of 9 per cent.)

The investigation of the alkali reserve of the cerebrospinal fluid cannot be replaced by that of the alkali reserve of the blood plasma in certain diseases because of the fact that in several pathologic conditions the relation between the results of the former and those of the latter is clearly and markedly disturbed.

SIGNORELLI, New Orleans.

DETERMINATION OF ADULTERATION OF BREAST MILK. M. KAYSER, München. med. Wchnschr. **82**:1447 (Sept. 6) 1935.

Many new stations for the collection of breast milk have been opened in Germany in the last few years. It is necessary to guard against adulteration of the breast milk with either water or cow's milk. Human milk examined under the ultraviolet rays has a characteristic color, which varies slightly for each woman. Another method to detect adulteration with cow's milk is to determine the acidity. Cow's milk requires from three to four times as much tenth-normal sodium hydroxide for neutralization as breast milk. Adulteration with water can be detected by measuring the specific gravity. Breast milk has a specific gravity of 1.030 or more.

BRAHDY, Mount Vernon, N. Y.

REVIEW OF STUDIES ON THE VIABILITY OF PATHOGENIC BACTERIA IN MILK. A. M. WAHBY, J. Egyptian M. A. **18**:623 (Sept.) 1935.

Wahby divides his review into a consideraton of: (*a*) the viability of pathogenic bacteria in sour dairy products, and (*b*) the viability of pathogenic bacteria in sweet milk products. In regard to (*a*) there seems to be no harmony of opinion, as experiments on similar enteric organisms kept at similar degrees of acidity under various temperatures for various lengths of time by different investigators have given conflicting results. This phase would bear more investigation. Under (*b*) the results, in contrast, have been uniformly the same, the enteric organisms may survive in milk, butter or even in ice-cream kept at a temperature of 4 F., in some instances as long as two years and four months. They survive in milk longer than in water. The various results "leave one convinced of the fact that the presence of typhoid-paratyphoid group in milk and its products creates a public menace."

MULHERIN, Augusta, Ga.

Vitamins; Avitaminoses

CAN AZOTOBACTER CHROOCOCCUM SYNTHESIZE VITAMIN D? J. E. GREAVES, J. Bact. **30**:143 (Aug.) 1935.

Azotobacter chroococcum, together with other nitrogen-fixing micro-organisms, possesses even greater synthetic powers than do higher plants, in that it can build complex organic compounds, including proteins, from elementary nitrogen and inorganic salts, provided a suitable source of energy is available. Hence, it seems reasonable to expect that this organism may be able to synthesize vitamin D or its precursor from such a simple substrate.

Azotobacter chroococcum was cultured on synthetic mediums consisting of inorganic salts and mannitol and tested for vitamin D and its precursor by feeding to rats. Greaves concludes from the results of the line test, the phosphorus content of the blood and the composition of the bone ash that Azotobacter chroococcum synthesizes from this simple medium the precursor of vitamin D, which is readily transformed into vitamin D by irradiation. This finding places this micro-organism with Clostridium butyricum (Heiduschka and Lindmen, 1929), Staphylococcus albus (Gerard, 1895) and the higher plants (Bills, 1935) in being able to synthesize ergosterol but unable to synthesize vitamin D. STOESSER, Minneapolis.

THE RECOGNITION OF SCURVY WITH ESPECIAL REFERENCE TO THE EARLY X-RAY CHANGES. E. A. PARK, H. G. GUILD, DEBORAH JACKSON and MARIAN BOND, Arch. Dis. Childhood **10**:265 (Aug.) 1935.

The most common early sign of scurvy in one hundred and twenty-five cases studied was a defect of the outer corner of the lower end of the radius. It appeared as a slight fuzziness of the cortex and slight rarefaction of the neighboring cancellous tissue. When this defect was more developed it took the form of a cleft underneath the lattice. Similar changes take place in the ankle.

The epiphyseal cartilage continues to produce new cells; that is, it continues to grow, even after the scurvy has developed. Growth in length of the long bones, therefore, keeps on unless the disease becomes so severe that even proliferation in the epiphysial cartilage stops. The practical significance of this is that in scurvy the cartilage keeps giving off its framework of matrix substance for the shaft to take over and form into bone.

Osteoblastic activity in the shaft and growth activity in the proliferative cartilage are distinct processes, carried on by different kinds of cells, apparently under different control. Although the cartilage cells divide and growth in length goes forward, osteoblastic bone formation stops and growth in thickness ceases. This means that new bone not only no longer forms on the surfaces of old bone but does not develop on the framework of calcified matrix substance which the cartilage keeps furnishing.

The most characteristic phenomenon in the roentgenogram in scurvy is the dense shadow lying across the end of the shaft. This shadow is cast by the scorbutic lattice.

In a clinical study of the one hundred and twenty-five cases of scurvy, in the majority of instances the condition occurred between 7 and 9 months of age. All the infants were artificially fed, most of them receiving boiled pasteurized milk. In 75 per cent of the cases the disease occurred in white infants. It required, on an average, about six months for the disorder to develop. The disease occurred chiefly during the summer months, reaching the peak (40 per cent) in September and October.

Excellent photomicrographs are shown, illustrating the histopathologic characteristics of scurvy, with roentgenograms showing the early signs of the disease.

KELLY, Milwaukee.

VITAMIN C AND ITS EFFECTS ON THE STRUCTURE OF THE TEETH. A. T. PITTS, Arch. Dis. Childhood **10**:295 (Aug.) 1935.

Experimental investigation of scurvy and the effects of this disease on the teeth of laboratory animals, notably the guinea-pig, resulted in fairly definite findings as reported by various workers. However, these findings cannot be applied to man. Scurvy, whether affecting adults or children, attacks the supporting structures of the teeth and leads to gingivitis and loosening. Florid scurvy of this type is rare.

Though the work of Hanke lacks complete proof, yet, taken in conjunction with the experimental work described, it suggests that vitamin C, as well as vitamins A and D, may be necessary to normal development and function of the teeth and that any deficiency of this vitamin in the diet may be reflected in lowered resistance of the teeth to disease. Since the average diet may easily be deficient in vitamin C, it is desirable to emphasize the importance of insuring a plentiful supply of this vitamin during the all-important years of childhood when growth of both the teeth and other tissues is most active and when the susceptibility to dental disease is greatest.

KELLY, Milwaukee.

THE VITAMIN C CONTENT OF THE LIVER OF NEWBORN INFANTS. K. U. TOVERUD, Arch. Dis. Childhood **10**:313 (Aug.) 1935.

The content of cevitamic acid (introduced as ascorbic acid) has been examined in the livers of fifty-six new-born infants, thirty-one of which were full term infants and twenty-five, premature infants.

The average value for the full term infants was 7.01 mg. per hundred grams of fresh liver, and for the premature infants, 6.05 mg., with variations of from 2.7 to 10.4 mg.

The early development of scorbutic symptoms, disappearing on antiscorbutic treatment, can be explained on the basis of a low congenital store of vitamin C in the organism. The time of development of symptoms of scurvy depends on the congenital store of vitamin C present and partly on the deficiency of the postnatal diet.

KELLY, Milwaukee.

INVESTIGATIONS INTO THE PATHOGENESIS OF SCORBUTIC DYSTROPHY. P. ROHMER and N. BEZSSONOFF, Arch. Dis. Childhood **10**:319 (Aug.) 1935.

A method of determining the amount of vitamin C in urine is described. It was found that infants fed a diet entirely free from vitamin C for two days continued to show vitamin C in the urine. This is in contrast to what occurs in older children and in adults. With infants over 1 year of age, the elimination of vitamin C fell to zero by the end of the first or second day.

Apparently, healthy infants are able to synthesize vitamin C. This function tends to decrease toward the eleventh month and is lost at the end of the first year. This method of investigation permits the study of the conditions under which the synthesis of vitamin C in the infant's body is inhibited.

KELLY, Milwaukee.

AVITAMINOSIS AND THE XEROPHTHALMIC SYNDROME. F. SCULLICA, Ann. di ottal. e clin. ocul. **63**:721 (Oct.) 1935.

After a thorough review of the literature, Scullica reports twelve cases observed in the clinic at Messina, Sicily, during the year 1931. In all the condition occurred during the months from October to December, inclusive. All the patients were babies from 2 to 5 years of age except one, a boy of 14. The diet after breast feeding was stopped consisted in all cases chiefly of bread or preparations of flour paste and dried beans. All but one of the children had shown signs of intestinal disturbance, usually with diarrhea. All showed marked loss of muscle tone and

more or less marked anemia, and a number had suffered from respiratory infections. Hemeralopia was present in ten of the children and was the symptom which called attention to the condition in most of them. Conjunctival xerosis was found in eleven of the patients. The corneal sensitivity was reduced in seven, but none showed other evidences of corneal involvement. Ten patients showed change in the fundus, usually a diffuse fine pigmentation at the periphery or about the disks.

All improved rapidly on cod liver oil or one of the vitamin A concentrates, the most improvement being seen with whole cod liver oil. The hemeralopia usually disappeared after a few days, while the xerotic patches required a number of months to heal. The changes in the fundus were not affected by treatment.

The intestinal disturbances were considered an important factor in bringing on avitaminosis. The changes in the fundus, which have not been described by most writers on the subject, are considered as the result of degeneration of the pigmented epithelium due to avitaminosis. GIFFORD, Chicago. [ARCH. OPHTH.]

CEVITAMIC ACID IN THE URINE. P. SCHIAPARELLI, Riv. di clin. pediat. **33**:795 (July) 1935.

Schiaparelli found that the breast-fed infant excretes in the urine less cevitamic acid (introduced as ascorbic acid) than the bottle-fed child.

Data on the excretion of cevitamic acid in the urine as reported in the scientific literature are plentiful but are unsatisfactory by reason of variations in the food and health of the children observed. Better controlled work is necessary for definite understanding of the metabolism of vitamin C. HIGGINS, Boston.

AVITAMINOSIS B IN CUBA. AUGUSTÍN CASTELLANOS, Bol. Soc. cubana de pediat. **7**:5 (Jan.) 1935.

Cases of avitaminosis B are not uncommon in Cuba. The children with this condition belong to the poorest classes, who are in great want and are always inadequately fed. Children of Negroes or mulattoes are mostly affected. The age ranges between 8 months and 4 years.

Undernutrition may extend over long periods; the diet is usually one-sided and contains a minimum amount of protein. The patients show great weakness and extreme wasting. Edema of the lower extremities, which eventually becomes generalized, is an early symptom. The principal sign—marked erythema of the edematous areas—appears next. This occurs in confluent patches. The erythema fades into a dark brown discoloration, and areas of desquamation appear over the affected parts. Neurologic symptoms and disturbance of motility then appear. Muscular weakness in the lower extremities almost equivalent to paresis is a prominent symptom. There is marked hypesthesia. The patient is dull, lethargic, depressed and often in a stupor. The condition is afebrile. There are few gastrointestinal symptoms. Rickets and xerophthalmia often are associated disorders. The prognosis depends on the progress of the disease. Recovery may take place rapidly if proper dietary measures are instituted. SCHLUTZ, Chicago.

INFANTILE AVITAMINOSIS IN THE STATE OF SÃO PAULO. VINCENTE BAPISTA, J. de pediat., Rio de Janeiro **2**:345 (Aug.) 1935.

There is a rather common form of mild rickets in São Paulo that affects all races alike. Scurvy is uncommon, as is deficiency of vitamin B_1 and of vitamin B_2.

SANFORD, Chicago.

THE BLOOD-AQUEOUS BARRIER AND VITAMIN C: I. THE PERMEABILITY OF THE BLOOD-AQUEOUS BARRIER AND THE CEVITAMIC ACID CONCENTRATION IN THE ANTERIOR CHAMBER. H. GOLDMANN and W. BUSCHKE, Arch. f. Augenh. **109**:205, 1935.

Large amounts of cevitamic acid (the reduced form of vitamin C) have been found in the normal aqueous of man and animals. Its concentration in rabbit

aqueous is about 20 mg. per hundred cubic centimeters. The vitamin C in the aqueous comes, for the most part, from the metabolism of the lens. The lens is known to reduce the oxidized form of vitamin C which enters the anterior chamber from the blood stream; but, in addition to this, the lens itself probably forms small amounts of the vitamin. As a result the concentration of the vitamin in the aqueous is about ten times that in the blood stream. It is known that vitamin C can diffuse freely from the blood into the aqueous, but the high concentration found in the aqueous suggests the possibility that this permeability is not reversible and that the aqueous-blood barrier normally prevents vitamin C from moving back into the blood stream from the aqueous.

Experiments were designed to test this hypothesis. Rabbits were used throughout. The concentration of vitamin C in the aqueous was determined by Harris' method. Special pipets were used to withdraw the aqueous from the anterior chamber so that it was never in contact with air except in the pipet itself. A preliminary series of experiments proved the concentrations of vitamin C equal in the two eyes in a series of normal rabbits. The permeability of the blood-aqueous barrier was increased by injecting sodium chloride subconjunctivally in concentrations of from 5 to 15 per cent. An increase in the concentration of protein in the aqueous and a more rapid appearance of fluorescein in the anterior chamber indicate to the authors that the injection of hypertonic solutions of sodium chloride effectively increases the permeability of the blood-aqueous barrier. They found a reduction in the vitamin C content of the aqueous in the majority of cases in which the hypertonic solutions of sodium chloride were employed. This reduction in the concentration of vitamin C did not run parallel with the increase in the protein content of the aqueous but followed more nearly the increase in the fluorescein in the anterior chamber. They regard the latter as a better indicator of permeability than the increase in the concentration of protein. Injections of epinephrine into a normal eye did not raise the concentration of vitamin C in the aqueous but, on the contrary, sometimes lowered it. Intramuscular injections of theophylline also lowered the concentration of vitamin C in the aqueous.

Goldmann and Buschke conclude that the blood-aqueous barrier normally prevents the reabsorption of vitamin C from the aqueous into the blood but that when the permeability of this barrier is increased vitamin C is rapidly reabsorbed into the blood stream. They discuss the possible relation which this may have in the production of cataract, more particularly cataracta complicata, in which they believe the inflammatory process (uveitis) may so increase the permeability of the blood-aqueous barrier that the vitamin C necessary for the metabolism of the lens disappears from the aqueous and the lens becomes opaque.

ADLER, Philadelphia. [ARCH. OPHTH.]

USE OF AN OINTMENT IN SHORTENING THE TIME OF IRRADIATION IN THE TREATMENT OF RICKETS. HANNS KRAFFT, Monatschr. f. Kinderh. **61**:107, 1934.

A favorable report is given of the use of a proprietary remedy which protects the body against heat but does not interfere with the effect of ultraviolet radiation. The use permits more intensive treatment.

GERSTLEY, Chicago.

Hygiene; Growth and Nutrition; Public Health

BODY MEASUREMENTS OF JAPANESE CHILDREN BORN IN AMERICA. P. M. SUSKI. California & West. Med. **43**:208 (Sept.) 1935.

Tables are presented which show the standard average values for height and weight, as well as Rohrer's index, for American-born Japanese children between the ages of 6 and 20 years. The averages are based on some 2,232 measurements, which were taken on about 800 children attending private Japanese schools in Los Angeles.

MARSHALL, San Francisco.

OBSERVATIONS ON THE PUBLIC HEALTH OUTLOOK. FRANK J. JIRKA, Illinois M. J. **68**:140 (Aug.) 1935.

Jirka points out that statistics of recent years indicate that the present efforts which are used in combating tuberculosis may not be sufficient to cause a continuance in the decline in the prevalence and mortality of that disease. Unfavorable economic conditions have served to handicap the good work that sanatoriums and medical and nursing services have been doing. He believes that some changes and modifications in the campaign against tuberculosis may be necessary for progress with satisfactory speed toward the goal of complete eradication.

The author advocates two improvements. One is the use of vaccination. The other is a closer, stronger and more comprehensive organization of the public health agencies and workers. He believes that the public health forces are the one outstanding example of unorganized effort in the field of general interests and public service. At the same time, they have the most useful and the most desirable commodity to offer in return for the support of their program.

Vaccination with BCG has gained progressive acceptance in France and many other countries and is beginning to be accepted in this country. A program has been planned and an organization has been arranged recently in Illinois with the view to giving BCG vaccine a fair trial, in the hope that it may aid in the campaign against tuberculosis in that state. BARBOUR, Peoria, Ill.

SYMPOSIUM ON PEDIATRICS; PLANNING A STATE WIDE SCHOOL HEALTH PROGRAM. FREDERICK L. PATRY, M. Rec. **142**:22 (July 3) 1935.

Patry believes that the following plan should be instituted in a state-wide school health program:

1. Service should be on a junctional rather than a geographic basis.

2. Local service facilities should first be identified and capitalized before remote help is called in.

3. The goal should be to decentralize services as soon as expedient so that each zone will have twenty-four hour service in specialized as well as in generalized help.

4. The aim to procure good supervision in every area where services are sought or rendered should be kept in mind.

5. It is illogical to use a specialist's time to do a generalist's work.

6. Every effort should be made to increase a more adequate preventive service in the field of mental hygiene.

7. Demonstration and training centers should be established at strategic points.

8. Experiences of each member of the Division of Health should be discussed with the rest of the group weekly.

9. Measures should be undertaken to encourage medical students and recent graduates to prepare for entry to such medical service as a life career.

10. The Division of Health needs more specialists to awaken an interest in at present overlooked conditions.

11. Each state should be divided into zones, and each zone should be equipped with its own permanent personnel. WILLIAMSON, New Orleans.

REPORT OF A STUDY OF LIGHTING IN SCHOOLS IN FAYETTE COUNTY, WEST VIRGINIA. GEORGE FORDHAM, West Virginia M. J. **31**:357 (Aug.) 1935.

A study of lighting conditions in fifteen schools in mountainous coal-mining districts in Fayette County, W. Va., is reported.

The study was made on bright sunshiny days in October 1934. The measurements were made by the most modern instruments, and the technical work was done by an electrical engineer. The measurements were recorded in foot-candles.

The General Electric Company recommends 20 foot-candles as a minimum illumination intensity. Of all these schools investigated, only 20 per cent had sufficient lighting. Only one building had adequate lighting, while one school had but 1 foot-candle of illumination intensity, which could, with the present equipment, be increased to only 2 foot-candles by artificial means.

The maximum lighting throughout the forty-eight states of the Union by sunlight used to its practical limit is only 58 per cent. This shows the necessity of constant additional lighting by artificial means.

SHAWKEY, Charleston, W. Va.

THE GROWTH CURVE OF AUSTRALIAN INFANTS DURING THE FIRST YEAR OF AGE: II. A COMPARISON—NORTH QUEENSLAND, TASMANIA AND NEW SOUTH WALES. F. W. CLEMENTS, M. J. Australia **2**:182 (Aug. 10) 1935.

Clements has constructed a chart for weight for infants in North Queensland from a study of 198 charts. He compared it with curves for weight of infants in Tasmania, where 246 charts were used. He found that there is no appreciable difference and concludes that the curve for growth of infants in Australia is not appreciably influenced by geographic distribution. TENNEY, Madison, Wis.

DEVELOPMENT OF THE THORAX: ITS SEMESTRIAL INCREASES DURING PUBERTY IN BOYS AGED FROM THIRTEEN TO EIGHTEEN YEARS. PAUL GODIN, Bull. Soc. de pédiat. de Paris **32**:713 (Dec.) 1934.

An anthropometric study of the thorax in boys during puberty was made. One hundred boys were measured regularly every six months from the age of 13½ to that of 17½ years. The values for the diameter at five levels of the thorax and the circumference at three levels were recorded, and the total increases in these measurements during the four years, as well as the periods of maximum and minimum increases, were determined. BENJAMIN, Montreal, Canada.

PRODUCTION OF LOW COST DWELLINGS IN PARIS IN THE SOCIAL DOMAIN. Y. DE HURTADO, Rev. méd.-sociale de l'enf. **3**:27 (Jan.-Feb.) 1935.

The architects of Les Office Publics des "Habitations à Bon Marché" (Offices for Production of Low Cost Dwellings) designed six or seven story buildings with apartments of various sizes, from those of a single room to those of four rooms and a kitchen, to rent at low rates. Preference is given to families whose dwellings are to be wrecked for public uses or because they are unsafe, to persons lodged in hotels and to persons who are without homes or are staying with parents or in homes consisting of only one or two rooms.

In January 1933 there were 59 groups of low rent buildings in Paris, representing the following classes: 12,185 lodgings of cheap rent, 3,047 apartments of moderate rent and 2,984 lodgings of rent intermediate between the two. Projects providing for 6,580 supplementary lodgings were also approved.

Twenty-one kindergartens are installed for the children from these buildings. Two thousand and five hundred children from 2 to 6 years old are taught by a special corps of teachers and are under the supervision of a physician, who records their physical and mental progress at least once a year. There are infant welfare services and facilities for bathing babies in the kindergarten, which serve as a means of interesting and educating the mothers in infant hygiene.

A medicosocial service has been set up to supervise the health, education and social needs of these tenants. In spite of such work it is only in the better class buildings with more interested and intelligent families that the infant mortality rate and incidence of tuberculosis are lowered below those of the general population. The author believes that in eight or ten years these methods will more than prove their worth and that the low cost rooms and apartments offer many advantages over the former wretched dwellings. SHAW, Evanston, Ill.

REACTION OF THE EMBRYO TO CHEMICAL AGENTS. K. BAUER, Virchows Arch. f. path. Anat. **294**:476, 1935.

Sixty pages with thirty-four illustrations are devoted to the presentation of work done in Held's institute for anatomy at Leipzig on the tissue reactions of the embryo to certain chemical agents. Forming the basis of the investigation was the concept that multiplication of the cells of the tissues of the adult organism, such as occurs in regeneration, inflammation and neoplasia, is dependent on a return of differentiated cells to the embryonic state or that it results from the activity of previously slumbering and indifferent embryonic cells. How the cells of the embryo react to agents that set up inflammation in the adult organism has, however, received scant attention. Bauer used the chick embryo as the object of study. The agents used were benzene, a benzene-paraffin mixture, aniline and aluminum powder. After a short period of incubation of the egg a small opening was made in the shell, the selected material was introduced, the opening sealed, and the incubation continued for from twenty-four to forty-eight hours. The embryos were then fixed and examined in serial sections. The localized granular degeneration and death of cells confirmed an older opinion that the embryo reacts to injurious agents only by degenerative processes and necrobiosis. But in portions of the embryo not killed by the chemical agents the ectoderm, the entoderm and the supporting mesenchyme of the mesoderm were hypoplastic, supposedly as the result of inhibition of growth by the chemical. The formation of blood vessels and hematopoiesis, however, were not inhibited and were more active than normal. Bauer could find no support for Maximow's view that indifferent mesenchymal cells participate in the formation of blood vessels. He believes that blood vessels come only from vascular endothelium. He discusses the relation of differentiation and cell division in the light of his observations. Cell division is not a function of the nucleus alone but is influenced by the cytoplasm. This influence may be an important feature in the proliferation of tissue when the stimulus to division is an abnormal one.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

RELATIVE CENTER OF GRAVITY IN BOYS AND GIRLS. ADOLF BASLER, Ztschr. f. menschl. Vererb. u. Konstitionslehre **19**:90, 1935.

The location of the center of gravity in relation to the measurements of the body was ascertained for 507 girls of from 6½ to 17½ years of age and for 438 boys aged from 6½ to 14½ years. The figures varied in the girls between 52.25 and 65.74 per cent of the height above the ground, the average for any one age being between 55.43 and 57.55 per cent. The center of gravity was found to be relatively nearer the ground as the age increased. In boys the value lay between 52.76 and 62.60 per cent of the height above the ground, with an average at a given age of from 56.22 to 57.29 per cent. No definite relation exists in boys between age and the center of gravity.

VINTON, New York.

ON THE INFLUENCE OF THE MEDICAMENTS INJECTED INTO THE FEMALE RABBIT UPON THE DEVELOPMENT OF THE FETUSES, ESPECIALLY UPON THE GROWTH OF THEIR EPIPHYSEAL CENTRES OF LONG BONES OF THE LIMBS AND THE BONES. E. TERADA, Jap. J. Obst. & Gynec. **18**:396 (Oct.) 1935.

Preparations of arsenic, iron and calcium were given intravenously to three groups of rabbits: to group A two months before conception and during pregnancy; to group B two months before pregnancy, and to group C during pregnancy. With iron and calcium the young of groups A and C showed a slight increase in bony growth. With arsenic the young of group B had better osseous development at birth than those of group A or of group C.

ADAIR and POTTER, Chicago.

Prematurity and Congenital Deformities

CONGENITAL DEFECTS. D. P. MURPHY, J. A. M. A. **106**:457 (Feb. 8) 1936.

In order to throw light on the question of the subsequent incidence of congenitally malformed children of parents having a defective child a study was made of a consecutive series of families each having a defective child. Among 275 such families interviewed, 34, or 12.4 per cent, gave rise to one or more additional congenitally malformed members. Among 43 conceptions that followed the birth of a malformed child, 331, or 76.8 per cent, normal full term offspring resulted. In the remaining 100 conceptions, or approximately 1 in 4, there were 43 (10 per cent) congenitally malformed children, 42 miscarriages (including abortions), 9 premature births and 6 stillbirths. In these families a second malformed child was born once in every 8.9 births, as compared with the incidence for the general population of 1 in every 213 births. It is concluded that congenital malformations serious enough to be recorded on birth certificates are approximately twenty-four times as likely to occur in families containing a congenitally malformed child as in the population at large.

BONAR, Salt Lake City.

GARGOYLISM (CHONDRO-OSTEO-DYSTROPHY, CORNEAL OPACITIES, HEPATOSPLENOMEGALY, AND MENTAL DEFICIENCY). R. W. B. ELLIS, W. SHELDON and N. B. CAPON, Quart. J. Med. **5**:119 (Jan.) 1936.

Reports are given concerning seven children who showed a remarkable resemblance to each other. The clinical features in each case were changes of the bone, a peculiar facies, congenital clouding of the cornea, distention of the abdomen with enlargement of the liver and spleen, and mental deficiency. Ellis, Sheldon and Capon call this syndrome gargoylism because the features suggest the appearance of gargoyles.

Ten additional cases from the literature are reviewed, and excellent photographs are appended.

BRADFORD, Rochester, N. Y.

ORTHOPEDIC CONSIDERATIONS IN THE TREATMENT OF SPINA BIFIDA. ROBERT S. SMITH, Surg., Gynec. & Obst. **62**:218 (Feb.) 1936.

A summary of fifteen cases of frank spina bifida and of thirty-six cases of spina bifida occulta is given. These lesions are associated with deformity of the feet of various types, congenital dislocations of the hip, scoliosis, incontinence of the bladder and the rectum, hydrocephalus and various trophic disturbances.

In general, the orthopedic treatment was directed toward the correction of deformities of the lower extremities by manipulation, wedging plasters, operations involving the tendons and arthrodesis of joints.

BUDSON, Detroit.

A CASE OF CONGENITAL SHORT NECK SHOWING THE KLIPPEL-FEIL SYNDROME. W. E. FOGGIE, Edinburgh M. J. **42**:421 (Aug.) 1935.

The special features of this syndrome are shortness or absence of the neck, giving a froglike and broad appearance; tenseness of the winglike trapezius muscles, and limitation of movements. Foggie reports the case of a 7 year old girl in whom the condition was discovered at birth. No one else in the family of three was affected. The child was undersized but well nourished; the head, which was large, seemed to be fastened on the trunk but remained bent forward. Photographs show these conditions. The child could move the head anteroposteriorly but little laterally. The dorsal part of the spine was rounded. A roentgenogram showed fusion of the bony column from the second cervical vertebra downward, for three or four vertebrae. The last cervical vertebra was free, but there was a cervical rib on the left side. The vertebrae seemed smaller than normal.

The discussion of cases reported in the literature brings out an interesting number of anatomic, nervous and mental derangements. Two other patients were found to be deaf-mutes; all sorts of malformations of the body have been reported as associated defects. The deformities are due to irregular segmentation of the spine in early fetal life as the result of injury.

NEFF, Kansas City, Mo.

MUSCULAR SPASM IN THE FOETUS A FACTOR IN THE PRODUCTION OF MALPRESENTATION. G. F. GIBBERD, J. Obst. & Gynaec. Brit. Emp. **42**:596 (Aug.) 1935.

Gibberd believes that, with the exception of extension of the legs in breech presentations, lack of the normal flexion of limbs or vertebral column while the fetus is in the uterus is due to spasm of extensor muscles.

He cites four cases in which roentgenograms taken at intervals of a few days showed a change in the position of the fetus but with an extended arm or hyperextended spine remaining constant. No abnormalities were noted after delivery.

ADAIR and POTTER, Chicago.

CONGENITAL ATRESIA OF THE DUODENUM. T. G. D. BONAR, Lancet **2**:822 (Oct. 12) 1935.

A case of duodenal atresia in a 13 month old girl is reported. The site of obstruction was exactly where the superior mesenteric vessels crossed the duodenum, and the common bile duct opened directly on to the posterosuperior aspect of the duodenum beyond the stricture. Because of enlarged glands on the head of the pancreas posterior gastrojejunostomy was the only feasible operation. The child died some hours after the operation.

According to Tandler, Forssner and Huerter, the vaterian segment of the duodenum is occluded by epithelial proliferation during the second month of fetal life, and atresia is due to failure of the plug to break down or become canalized. In this case canalization had apparently taken place, but one area had become replaced by fibrous tissue, which had gradually led to atresia.

LANGMAN, New York.

CONGENITAL HYPERTROPHY OF THE HEART? (CARDIOMEGALIA GLYCOGENICA): SPECIMEN. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:1330 (Aug.) 1935.

An infant of 4 months was admitted to the hospital with a history of never having cried normally and of growing more feeble. The child was fed by tube, but the breathing became more dyspneic, and death occurred. This was apparently due to respiratory paralysis.

Postmortem examination showed a firm, globular, enlarged heart weighing 73 Gm. The enlargement was due to hypertrophy of the left ventricle, for the most part.

The report of the results of histologic examination of the myocardium and of the gluteus maximus and gastrocnemius muscles, as well as photographs of the heart and photomicrographs of sections of the myocardium, accompany the report.

WILLIAMSON, New Orleans.

MILD FORM OF DYSCHONDROPLASIA. E. LESNÉ, J. A. LIÈVRE and G. LOISEL, Bull. Soc. de pédiat. de Paris **32**:354 (June) 1934.

A boy, 5 years old, was admitted to the hospital because of insufficient gain in height. He cut the first tooth at 8 months of age but did not walk until 20 months of age. He weighed 18.9 Kg. and measured 1.04 meters, which are normal figures for his age. His limbs were obviously short as compared with his trunk. Roentgenologic examination showed marked abnormalities of the right hand and, to a lesser extent, of the left hand. The ends of the diaphyses had irregular lines

which were notched; laterally, they had prominences which often resembled a bird's beak. The feet showed these abnormalities to some extent only in the metatarsal bones. The slight resemblance to achondroplasia which the child presented was not confirmed by the roentgenograms, as the long bones showed no abnormalities. The prominences at the ends of the bones of the hands which could be palpated resembled those observed in cases of multiple exostoses. It was considered that this case fitted best into the category described by Ollier as dyschondroplasia, of which it was classed as a mild form.

BENJAMIN, Montreal, Canada.

FUNNEL THORAX. OPERATIVE RESULT. L. OMBRÉDANNE, Bull. Soc. de pédiat. de Paris **33**:21 (Jan.) 1935.

A boy, 4½ years old, presented marked deformity of the chest. There was considerable depression of the sternum and of the right lateral costal region, and the left half of the chest bulged anteriorly. He had no respiratory symptoms but was subject to spells of a syncopal character which were considered to be due to cardiac abnormality. There was considerable deviation of the apex of the heart to the left, and the auricular areas bulged in the retrocardiac space on roentgen examination. It was considered that appliances and exercises could not improve the deformity, and operative measures were employed. The sternum and left costal cartilages were sectioned at the first sitting, and, after eleven days, during which the child had one of his usual fainting spells, the right costal cartilages were cut. Elastic traction was applied for twenty-two days, after which it was removed and breathing exercises were begun. Ten days later the child was allowed to be up. The former depression of the wall of the chest was filled out.

BENJAMIN, Montreal, Canada.

REPORT OF A CASE OF CONGENITAL ATRESIA OF THE DUODENUM. JUAN A. ALONSO MUÑOYERRO and ANGEL ALIQUE, Pediatría españ. **24**:137 (April) 1935.

Congenital atresia of the duodenum, an unusual anatomic defect, occurred in a new-born infant, first seen on the sixth day. The abnormality was not recognized until after death, which occurred on the eighth day. Atresia was found above and below the duodenum. The stomach showed hour-glass constriction.

The authors point out the importance of roentgenologic examination in such cases and state that it is almost impossible to establish the diagnosis without it.

SCHLUTZ, Chicago.

A STUDY OF STILL BIRTHS IN 3,974 CONSECUTIVE DELIVERIES IN THE FIRST NATIONAL MIDWIFERY SCHOOL MATERNITY HOSPITAL. MARION YANG and H. H. HUANG, Chinese M. J. **49**:755 (Aug.) 1935.

The authors report figures from the Department of Public Health of Peiping Union Medical College and the Central Field Health Station of Nanking, covering a period of four years. The number of stillbirths per thousand live births was 55.2. Trauma at birth accounts for the largest number, 53.3 per cent. The ratio of stillborn boys to stillborn girls was 65.6:44.6. For the infants of mothers who had received some antepartum care the stillbirth rate was 17.2; in those cases in which the mothers had received no antepartum care there were 409.2 stillbirths in 3,974 consecutive deliveries.

NEFF, Kansas City, Mo.

New-Born

INCLUSION BLENNORRHEA. S. H. MCKEE, Am. J. Ophth. **18**:36 (Jan.) 1935.

McKee discusses epithelial cell inclusions and describes inclusion blennorrhea as a "new disease" occurring in infants and resembling gonoblennorrhea. The prognosis, however, is good. He examined twenty-seven cases of ophthalmia of

the new-born and found epithelial cell inclusions in seventeen cases. In eight of these cases they were combined with gonococci and in one case with streptococci. He found gonococci alone in five of the seventeen cases and streptococci or pneumococci alone in five cases. He discusses the inclusion bodies found in trachoma, inclusion blennorrhea and swimming pool conjunctivitis. He concludes with Stewart that the inclusion is formed by phagocytosis of bacteria which are not the cause of these diseases but which carry the viruses.

REESE, Philadelphia. [ARCH. OPHTH.]

PROBLEMS OF THE NEW-BORN—A CLINICAL VIEWPOINT. WARREN QUILLIAN, Arch. Pediat. **52**:761 (Nov.) 1935.

Not abstracted. WADDELL JR., University, Va.

CYANOSIS OF THE NEW-BORN. E. A. MORGAN and ALAN BROWN, J. A. M. A. **105**:1085 (Oct. 5) 1935.

Cyanosis of the new-born constitutes a problem which has received in the past too little attention from the obstetrician, general practitioner and pediatrician. Aspiration of mucus, with resultant impairment of ventilation, is the most common cause and one that can be corrected by careful removal of the pharyngeal secretions before the onset of respiration. Cerebral edema is a distinct clinical entity and an important cause of cyanosis. Intracranial hemorrhage, another cause of cyanosis, is difficult to diagnose, owing to the lack of a clearcut definition and the need of more uniformity in the interpretation of the various diagnostic procedures. Enlargement of the thymus may be a cause of cyanosis, but so far no factual proof of such a relationship has been forthcoming. Tetany is considered a frequent cause; this should not be overlooked, because it responds to specific therapy.

BONAR, Salt Lake City.

SOME INTERESTING CASE REPORTS. G. P. NEEL, South Carolina M. J. **31**:243 (Dec.) 1935.

A baby boy 4 days and 15 hours of age had a distended abdomen, with a history of diarrhea and restlessness since birth. On operation a well walled-off abscess was found, from which were removed pus, fiber and meconium. Complete recovery followed. The diagnosis was appendiceal abscess, probably existing from birth.

WESTON JR., Columbia, S. C.

THE PREVENTION OF BIRTH INJURIES. CALVIN R. HANNAH, South. M. J. **28**:1021 (Nov.) 1935.

Hannah believes that injury to the fetal brain may not be the fault of the delivery but may be due to failure of the brain cells to develop from faulty germ plasm. Premature babies are more easily injured than full term babies because of the incomplete development of the blood vessels, which are fragile and easily broken. The correct type of delivery may prevent injury to the brain. Central episiotomy done with solid blade forceps is the safest type of delivery for a premature baby.

SCHLUTZ, Chicago.

URINARY DISORDERS OCCURRING IN THE NEONATAL PERIOD. W. S. CRAIG, Arch. Dis. Childhood **10**:337 (Oct.) 1935.

Sixty-one new-born infants with urinary disorders are described. The urinary findings are compared with those in a series of healthy new-born children. Prolonged anuria, fever, restlessness, pallor and the presence of pus and organisms in the urine reveal urinary disease. Forty boys and twenty-one girls comprised the series. There were nine deaths in the series. In the fatal cases in which the patient came to autopsy, the pathologic changes were slight and were most often noted in the renal substance, rarely in the pelvis.

The symptoms are closely related to the excretory activity of the kidneys, and treatment should be directed toward the promotion and maintenance of adequate diuresis. This is best attained by the giving of fluids at frequent intervals and the administration of alkalis and weak tea. Recovery is usual. A follow up of the children after their discharge from the hospital showed that recovery was complete. Remissions rarely occurred, and the subsequent general health of the children was not impaired.

KELLY, Milwaukee.

BLOOD COUNTS OF NEWBORN INFANTS IN RELATION TO ICTERUS NEONATORUM. L. C. MARTIN and S. M. EVANS, Arch. Dis. Childhood **10**:355 (Oct.) 1935.

Blood counts were made over a period of five days on twenty normal infants born at full term. Icterus neonatorum developed in nine of the infants. The erythrocyte count at birth bears no relationship to development of icterus neonatorum. The average five day erythrocyte curve of icteric infants is higher, and that of nonicteric infants is lower, than the average curve in all cases. No conclusion as to the occurrence of icterus neonatorum can be drawn from the five day curve for an individual infant. Icterus neonatorum is an expression of temporary lack of balance between the production and destruction of erythrocytes. Average values are given for cell counts and the hemoglobin estimations of newborn infants. Infants born by cesarean section show a slightly lower average erythrocyte count and hemoglobin estimation than infants born naturally.

KELLY, Milwaukee.

PNEUMONIA AND OTHER COMMON RESPIRATORY CONDITIONS IN THE NEW-BORN. W. S. CRAIG, Edinburgh M. J. **42**:599 (Nov.) 1935.

In routine postmortem examinations during two years Craig has observed a high incidence of hemorrhagic and inflammatory lesions of the lungs. The fact that symptoms were present during life suggests that such morbid changes might be recognizable clinically.

The infants were born in the Royal Maternity Hospital and were under observation for four weeks after birth. When they showed evidences of distress or disturbance they were subjected to a complete physical examination. An attempt was made to arrive at a diagnosis; symptoms indicating respiratory involvement were contrasted with absence of clinical evidence of pulmonary involvement.

At the one hundred and forty-six autopsies a number of the new-born had normal and well expanded lungs. Pneumonia was present in forty-five infants; in three of these there was associated bronchitis, and in eight, associated intrapulmonary hemorrhage. There was intrapulmonary hemorrhage in fourteen infants who had no associated inflammatory lesion. A large number had extensive uncomplicated atelectasis.

The clinical study of the various pathologic conditions showed much similarity, but each had some characteristic feature. Atelectasis had been diagnosed usually; in some infants it was only suspected, while in a few it was overlooked. Bronchitis had been diagnosed in the few patients who died of it. In pneumonia and pulmonary hemorrhage the pictures were similar, so that the two conditions could not be differentiated. Consolidation was usually diagnosed but was not detected when inflammation or hemorrhage was so small that microscopic section was necessary to recognize it.

In infants, especially the premature who are born asphyxiated, respiratory disorders are likely to develop and to be associated with cerebral hemorrhage.

In atelectasis the breathing, if "cogwheel" or "ratchet," is diagnostic. Over the areas of pneumonia or intrapulmonary hemorrhage there are fine crackling râles of a peculiar nature, which indicate consolidation and are present in no other respiratory diseases of the new-born.

Cyanosis recurs as a constant finding when there is pulmonary consolidation. It is benefited by the administration of oxygen, which is not true for the cyanosis due to intracranial hemorrhage, sepsis, pyelitis or atelectasis. Pulmonary consolidation is usually fatal within a few days. NEFF, Kansas City, Mo.

CHARACTERISTICS OF THE CAPILLARY LOOPS OF THE PAPILLAE OF THE SKIN IN THE NEW-BORN. G. SALVIOLI, Riv. di clin. pediat. **33**:1093 (Oct.) 1935.

Salvioli presents photomicrographs of the capillary loops seen through the nail of the new-born. These loops are already formed at birth, both in the child at term and in the premature infant. There are two types of loops, the long type and the short type. With development the capillaries seem to increase in number rather than in size. HIGGINS, Boston.

BLOOD OF THE NEW-BORN. CLEMENTE INCLÁN and VICTOR SANTAMARINA, Arch. de med. inf. **4**:125 (Sept.) 1935.

The authors studied the hemoglobin, erythrocytes and white cells and the bleeding time and coagulation time of the new-born. Ten interesting photomicrographs of the kinds of white cells noted are shown. The results do not differ materially from those of other investigators. SANFORD, Chicago.

TREATMENT OF ASPHYXIA OF THE NEW-BORN. WALDYR DE ABREU, Rev. de gynec. e d'obst. **28**:458 (Sept.) 1934.

The mechanical and physical means of distention of the lungs and the medicinal means of direct stimulation of the respiratory center are considered. Spanking and the use of hot and cold water, mixtures of oxygen and carbon dioxide, and special drugs, such as caffeine, metrazol and a preparation of lobelia, are mentioned. The author includes a drug which is a combination of two synthetic bases that are supposed to stimulate the respiratory center and the vascular system; he gives 1 cc. of a 0.5 per cent solution of this drug subcutaneously. Oxygen can be introduced by a catheter. HERRON, Spokane, Wash.

FETAL ASPHYXIA FOLLOWING ARTIFICIAL RUPTURE OF THE MEMBRANES. AFFONSO HENRIQUES FURTADO, Rev. de gynec. e d'obst. **29**:629 (Dec.) 1935.

The author describes a case of fetal asphyxia following artificial rupture of the membranes. The cord was inserted anomalously. As this may happen in 1 per cent of all deliveries, perhaps in many cases fetal asphyxia attributed to pressure on the head may be due to compression of the cord. SANFORD, Chicago.

LARGE MEDIASTINAL SHADOWS IN THE NEW-BORN. SIEGFRIED LIEBE, Monatschr. f. Kinderh. **64**:48, 1935.

Liebe reports the cases of three new-born infants, illustrated with roentgenograms showing large shadows in the mediastinum. The children suffered from cyanosis and dyspnea and showed some petechiae. Cardiac dulness extended to the midaxillary line, but no murmurs were present. Râles were heard in both lungs. After a few days the symptoms disappeared spontaneously.

The author believes that this condition is due to a muscular insufficiency of the heart, which develops under the strain of extra-uterine life. After a few days cardiac adjustment is accomplished.

The condition should not be confused with congenital heart disease.

GERSTLEY, Chicago.

Acute Contagious Diseases

SCARLET FEVER (SUSCEPTIBILITY AND ACTIVE IMMUNIZATION). SILBER C. PEACOCK, Illinois M. J. **68**:249 (Sept.) 1935.

From a statistical analysis of the results of the Dick test on 3,029 children at the Children's Memorial Hospital, from his experience with active immunization against scarlet fever and from a review of the experiences of other investigators, Peacock concludes that the Dick test is a good measure of susceptibility to scarlet fever in at least 90 per cent of the cases. The period of greatest susceptibility is from the first to the eighth year of life. The author also believes that five graduated injections of sterile commercial antitoxin given at about weekly intervals produce negative reactions to the Dick test in 90 per cent of susceptible subjects. From 10 to 20 per cent of those given injections experience marked local or systemic reactions. On the whole, the durability of the immunization has been very good.

BARBOUR, Peoria, Ill.

THE ANTIGENIC VALUE OF VARIOUS PREPARATIONS OF DIPHTHERIA TOXOID. C. E. HEALEY, J. A. M. A. **105**:1182 (Oct. 12) 1935.

It was concluded that toxoid prepared in the United States from 1929 to 1932 was about equal in its antigenic value to that prepared by Ramon in France in 1929 to 1934. From 1932 to 1934 there has been a decrease in the antigenic value of diphtheria toxoid in this country, while that of the French toxoid has remained the same. There is need, therefore, for better application of the present methods or for better methods for control of the antigenic value of diphtheria toxoid in this country.

BONAR, Salt Lake City.

THE REDUCTION OF DIPHTHERIA FOLLOWING THREE DOSES OF TOXOID. N. E. MCKINNON and M. A. ROSS, J. A. M. A. **105**:1325 (Oct. 25) 1935.

Previously it was reported that in the period of 1927 to 1930 when the corrected rates of diphtheria obtaining in the controls were applied to 16,829 children given three doses of toxoid in the Toronto public schools the expected cases numbered 222. Actually there were 23 cases, a reduction of 90 per cent, and no deaths.

Later observations on this group and on 29,029 additional children given three doses of toxoid subsequent to 1929-1930 showed that instead of 460 expected cases, as estimated for the whole period of 1927-1932, there were actually 40 cases, a reduction of 91 per cent. One death from diphtheria occurred in the 46,000 children immunized. Immunity is greatest the first year but remains at a high level—from 80 to 90 per cent—for at least four or five years.

BONAR, Salt Lake City.

DIPHTHERIA IMMUNIZATION OF ALLERGIC AND NONALLERGIC INDIVIDUALS BY INTRACUTANEOUS INJECTION OF ALUM-PRECIPITATED TOXOID. RICHARD A. KERN, JEAN CRUMP and THOMAS A. COPE, J. Allergy **6**:525 (Sept.) 1935.

The authors' summary is as follows:

1. A single intracutaneous injection of alum-precipitated toxoid is as successful as a subcutaneous injection in producing active immunity against diphtheria, and with a dose only one tenth of that usually employed in the subcutaneous method.

2. Immunization against diphtheria by the intracutaneous injection of the toxoid is distinctly less likely to produce unfavorable reactions, either local or general, than is that by the subcutaneous method.

3. Immunization against diphtheria by the intracutaneous injection of alum-precipitated toxoid should therefore be the method of choice, especially in allergic subjects.

HOYER, Cincinnati.

ELEMENTARY BODIES OF VACCINIA. R. F. PARKER and T. M. RIVERS, J. Exper. Med. **62**:65, 1935.

By differential centrifugation in the horizontal and angle centrifuges it is possible to obtain appreciable quantities of relatively pure elementary bodies of vaccinia. Such preparations of elementary bodies exhibit an extremely high titer of vaccine virus. The elementary bodies are specifically agglutinated by serum from rabbits immunized by injections of bacteria-free vaccine virus. Virus-free filtrates of dermal vaccine virus and of bacteria-free testicular vaccine virus contain a soluble substance or substances that are precipitated by antivaccinal serum.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

SCARLET FEVER IMMUNIZATION OF NURSES. GAYLORD W. ANDERSON and WARREN I. REINHARDT, J. Infect. Dis. **57**:136 (Sept.-Oct.) 1935.

Anderson and Reinhardt reported on 6,346 nurses in various hospitals in Massachusetts who were immunized against scarlet fever. The attack rate of scarlet fever among the nurses showing a positive Dick reaction and not immunized (susceptible) was 12.8 per cent; for the group of those having a negative Dick reaction and those who had shown a positive Dick reaction and were later immunized it was 0.7 per cent. The authors conclude that the Dick reaction is a reliable index to immunity, that five injections of Dick toxin can immunize a susceptible person and that the immunity lasts at least three years.

TOOMEY, Cleveland.

THE PROBLEM OF RABIES. WILLIAM B. GRAYSON and GORDON HASTINGS, South. M. J. **28**:924 (Oct.) 1935.

The stray dog is the primary factor in propagating and perpetuating rabies. Overcoming a misdirected sympathy for dogs is the chief problem in combating this disease. The passage and enforcement of stringent and effective laws regarding dogs is the only way of eradicating the disease. Licensing, quarantining, leashing, muzzling, vaccination, and destruction of all vagrant dogs are measures which, if vigorously applied, would eradicate the disease in a few months. These measures should be accepted as each accessory to the other.

SCHLUTZ, Chicago.

SUSPENSIONS OF ELEMENTARY BODIES FROM VACCINIA FILTRATES. G. H. EAGLES, Brit. J. Exper. Path. **16**:181, 1935.

A method has been described whereby large quantities of the virus of vaccinia, consisting of suspensions of elementary bodies, may be obtained. These suspensions are of high potency and are a valuable addition to the sources of bacteriologically sterile vaccine virus and may possibly find a place in the practice of vaccination. They produce typical vaccinal reactions in animals on intradermal inoculation and on scarification. These reactions are followed by immunity on subsequent vaccination.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

THE CULTIVATION OF VACCINIA VIRUS. G. H. EAGLES, Brit. J. Exper. Path. **16**:188, 1935.

The behavior of the virus of vaccinia in a medium apparently free from whole living cells has been further investigated. A number of series of subcultures are presented in detail. The difficulties encountered in previous experiments were again experienced. These are shown by the poor survival of the virus in large numbers of individual flasks and the inability to secure either growth or survival of the virus in a number of subcultures. Multiplication of the virus apparently took place in two of the series of subcultures. Possible sources of error in technic

and interpretation have been carefully considered and investigated. But no source of error has been identified which suggests that subcultures successful as judged by titrations may not be interpreted as evidence of growth in a cell-free medium.

FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

ANTI-SCARLATINAL SERUM IN ERYSIPELAS. W. H. BRAZIL, Brit. M. J. **2**:840 (Nov. 2) 1935.

A case of facial erysipelas in which antiscarlatinal serum was given by the intramuscular route is reported. The result was dramatic, improvement being pronounced and rapid.

ROYSTER, University, Va.

THE USE OF ALUM-PRECIPITATED TOXOID IN DIPHTHERIA IMMUNIZATION. J. E. HAINE, Brit. M. J. **2**:896 (Nov. 9) 1935.

Two districts were selected for this study. One was peculiarly likely to suffer invasion from infection because of the large number of summer visitors. The other district was far from sanitary and was likewise conducive to the spread of infection. A study was made to determine the value of a single injection of alum-precipitated toxoid. Haine recognizes the value of the follow-up Schick test but feels that it is exceedingly difficult to carry out this program in rural districts and that it is wiser to administer the toxoid to all supposedly susceptible children, whether or not the Schick test is subsequently done, feeling that it is better to have a small percentage of possibly susceptible children than it is to attempt 100 per cent immunization by requiring a subsequent Schick test. The author also casts some doubt on the absolute value of the Schick test, since he has seen diphtheria develop in a child with a negative Schick reaction.

ROYSTER, University, Va.

PREVENTION OF DIPHTHERIA BY THE "ONE-SHOT" METHOD USING ALUM-PRECIPITATED TOXOID. M. NAUGHTEN, J. H. WHITE and A. FOLEY, Brit. M. J. **2**:898 (Nov. 9) 1935.

This study was carried out on three groups of institutional children the average ages of whom were 10½, 11½ and 12½ years. There were certain reactions in this group, varying from the small painless induration to a rather generalized brawny induration, but even considering these reactions, which rarely occur in young persons, the author feels that the alum-precipitated toxoid is safe and advisable for this age group.

ROYSTER, University, Va.

A FATAL CASE OF PREGNANCY COMPLICATED WITH MUMPS. P. C. DUTTA, J. Obst. & Gynaec. Brit. Emp. **42**:869 (Oct.) 1935.

A primigravida, aged 18, suffered from an attack of mumps in the eighth month of pregnancy. On the fifth day of the disease generalized edema, marked albuminuria and oliguria occurred. The condition became progressively worse. A dead fetus was delivered on the eighth day of the illness, and death occurred on the eleventh day.

Mumps constitutes a grave complication of pregnancy and may produce acute nephritis causing death in both the fetus and the mother.

ADAIR AND POTTER, Chicago.

TREATMENT OF DIPHTHERIA. I. H. ALANTAR, Arch. de méd. d. enf. **38**:676 (Nov.) 1935.

In a discussion of the specific treatment of diphtheria as observed in the children's wards at Istanbul, the author offers the following conclusions:

The diagnosis of diphtheria should be made clinically, laboratory aids being utilized only as a secondary check. Injections of serum should be made only on

clinical indications. The dose should be calculated in units per kilogram of body weight. From 300 to 600 units per kilogram of body weight according to the severity of the case, is recommended, as advised by Pirquet and Schick. Only the most concentrated serum should be employed, and a single injection should be used, repeated injections being used only in severe cases. In ordinary cases the serum should be injected intramuscularly; in severe cases the serum should be injected half intramuscularly and half intravenously. The use of specific serum should be accompanied by cardiac tonics, and surgical procedures must be invoked promptly in membranous croup.

AMESSE, Denver.

BACTERIOLOGIC STUDY OF MALIGNANT DIPHTHERIA. ROBERT POINSO, Bull. Soc. de pédiat. de Paris **33**:47 (Jan. 15) 1935.

Cultures were made from the throat in sixty-one cases of severe diphtheria. The bacilli observed were of the long, medium and short types; in some cases a single type occurred, and in others a combination of different types was obtained. The majority were of the long type. It is concluded that virulence cannot be judged from the length of the bacilli. Streptococci and Staphylococci are often noted in association with diphtheria bacilli, but no definite rôle can be ascribed to their presence. It is pointed out that swabs of material from the throat must be taken from the edge of the membrane carefully; otherwise, cultures made from them may not show diphtheria bacilli, and this is especially true in cases in which associated cocci are present on the surface of the membrane. In cases in which diphtheria is diagnosed clinically, antitoxin should be administered without waiting for the findings in a culture from the throat or even if a culture does not show diphtheria bacilli.

BENJAMIN, Montreal, Canada.

A CASE OF ENCEPHALITIS FOLLOWING VACCINATION. R. PIERRET and A. BRETON, J. de méd. de Paris **55**:784 (Sept. 5) 1935.

A child 9 years old, thirteen days following a vaccination, which had been followed by some edema and by pustules and adenitis, became acutely ill, showing convulsions and delirium. Coma followed, from which the child did not recover. The temperature was about 41 C. (105.8 F.), and death occurred on the third day. Lumbar puncture showed no abnormality. Postmortem examination was not made.

LESLIE, Evanston, Ill.

TRACHEAL OBSTRUCTION IN A CHILD TRACHEOTOMIZED FOR DIPHTHERIA; RECOVERY FOLLOWING BRONCHOSCOPY. DURIEU and LEROY, J. de méd. de Paris **55**:848 (Sept. 26) 1935.

A child 2 years old who was tracheotomized for laryngeal diphtheria two days later had a tracheal obstruction which could not be relieved by the habitual procedures. With the child already in a state of pre-agonal asphyxia, bronchoscopy was resorted to. A large mass consisting of an agglomeration of false membranes and secretions was removed, with immediate improvement in the condition of the child.

LESLIE, Evanston, Ill.

HISTOLOGIC LESIONS AND THE SIGNIFICANCE OF THE SCHICK REACTION. A. SÉZARY, LÉVY-COBLENTZ and CHAUVILLON, J. de méd. de Paris **55**:916 (Oct. 17) 1935.

This is, primarily, a study of the histologic difference between lesions of allergy and lesions due to toxin. The former show considerably more necrosis. If details are desired the article should be read in full.

LESLIE, Evanston, Ill.

DIPHTHERIA OF THE PENIS AND OTHER REGIONS. MARTÍNEZ VARGUS, Med. de los niños **36**:353 (Dec.) 1935.

Diphtherial infection occurs infrequently in regions distant from the faucial and nasal cavities. The author has seen mastoidectomy wounds with a diphtheritic membrane and, in one instance, a child with conjunctivitis due to diphtherial infection, which resulted in a completely opaque cornea, with loss of vision. The recent literature on this subject is reviewed. Four unusual cases were reported during the present year, two of diphtheria of the vulva, and two of diphtheria of the penis following circumcision, reported by Borovsky in *The Journal of the American Medical Association.*

DWYER, Kansas City, Mo.

NASAL DIPHTHERIA. HUMBERTO COOPER ALFARO, Rev. chilena de pediat. **6**:362 (Aug.) 1935.

Nasal diphtheria is of frequent occurrence, judging from the experience of the author, and was present in more than one third of the cases of diphtheria in his clinic. It can occur in the ambulatory patient. The author considers it one of the principal factors in the transmission of diphtheria. The nose and rhinopharynx are the principal seat of the Klebs-Löffler bacillus and the point from which it extends to other regions.

SCHLUTZ, Chicago.

HISTOPATHOLOGY OF EXPERIMENTAL POSTVACCINAL ENCEPHALITIS. J. SANZ IBÁÑEZ and A. P. RODRÍQUEZ PÉREZ, Trav. du lab. de recherches biol. de l'Univ. de Madrid **29**:167, 1934.

Sixteen rabbits were killed twenty-four, forty-eight, seventy-two and ninety-six hours after intracerebral injections of the encephalic virus of Gallardo. As a result of the study of the brains the following conclusions were reached: (1) An etiologic relationship exists between the vaccinal virus and the lesions of the central nervous system; (2) neuronal alterations of degenerative nature occur in the form of hyperchromemia and vascular degeneration; (3) the porencephalic cavities are due to the action of the virus; (4) perivascular infiltrations do not occur; (5) the neuroglia react with hypertrophy and gliosis; (6) the macroglia appear to migrate to the region of the lesion; (7) there is no specific microglial reaction due to the virus, the changes in these cells being due to necrosis of cerebral tissue; (8) the reaction of the virus is essentially ectodermal; (9) the myelin and oligodendroglia show no reaction to the virus, and (10) a meningeal reaction is interpreted as being a response to the virus. The article has an excellent bibliography.

COURVILLE, Los Angeles. [ARCH. PATH.]

RESISTANCE OF THE NEW-BORN TO VACCINATION. JOSEF VON LUKÁCS and DÈNES VON MÓRITZ, Arch. f. Kinderh. **105**:1, 1935.

The new-born infant is relatively resistant to vaccination against smallpox. The reaction develops more slowly than in the older infant. The papilla is larger, but the areola is small, and there are almost no general symptoms. This difference in reaction is due to the absence of allergic sensitivity in the newborn.

CRANE, Chicago.

MACROSCOPIC DIAGNOSIS OF DIPHTHERIA ON "BLOOD-TELLURIUM SULFHYDRYL AGAR." JOACHIM TIETZ, Deutsche med. Wchnschr. **61**:834 (May 24) 1935.

A blood-tellurium-sulfhydryl agar medium prepared with sheep's blood is proposed for the quick diagnosis of diphtheria based on morphologic features of colonies. The time required for the growth is twenty hours. This method of culturing yielded one and a half times more positive results than the Loeffler method, when tested in 1,000 parallel examinations. Whenever the results of the

new method did not check with those of the Loeffler method, further study and animal experiments showed that the results obtained with the blood-tellurium-sulfhydryl agar method were more reliable. The growth of diphtheria bacilli obtained might show three different types of organisms morphologically. Anderson and his co-workers claimed that one can draw conclusions from these three types of morphologic features of colonies as to the pathogenicity of the organism. However, this contention needs further verification. The author claims the following advantages for the blood-tellurium-sulfhydryl agar method of macroscopic diagnosis of diphtheria as compared with the Loeffler method: (1) simple preparation of the medium, (2) great sensitivity of the medium for diphtheria bacilli, (3) shortening of the time of growths, (4) reliability and specificity of the morphologic features of the colonies and (5) different types of morphologic features of colonies among different strains of true diphtheria bacilli.

KERESZTURI, New York.

THE SCHICK TEST AND ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. M. GUNDEL and WÜSTENBERG, Deutsche med. Wchnschr. **61**:1871 (Nov. 22) 1935.

Active immunity was produced in 4,000 children with from one to three injections of diphtheria toxoid or with diphtheria toxin-antitoxin. From six to twelve months after immunization from 2.5 to 5 per cent of the subjects reacted positively to the Schick test. Among the nonimmunized children in the same communities in which the immunizations were carried out, 12.8 per cent were found to have a positive Schick reaction and in Brandenburg, where no active immunization was attempted, 26 per cent had a positive Schick reaction. No difference could be demonstrated between the efficacy of the toxoid and that of the toxin-antitoxin. The morbidity and mortality from diphtheria were lower in the immunized groups. The comparative value of one, two and three injections was not obvious.

KERESZTURI, New York.

OLD AND NEW PROBLEMS IN DIPHTHERIA. H. OPITZ, Kinderärztl. Praxis **7**:25 (Jan.) 1936.

This is an interesting review involving mainly problems concerned with the continued increase in the number of cases of diphtheria in Germany and with the increasing frequency of cases of the so-called toxic forms, in which there is a mortality rate of about 50 per cent. According to Opitz, this cannot be explained by climatic conditions, by differences in race or nutrition or by delay in the administration of serum. Usually such forms start with toxic symptoms. The increase in the number of cases of these malignant forms runs parallel with a marked decrease in the number of cases of diphtheritic croup (from 30 to 1 per cent). The occurrence of postdiphtheritic paralyses was independent of the doses of serum given and was observed in 12 per cent of the cases. The value of active immunization against diphtheria still does not seem to be considered to be proved in Germany.

HEYMANN, Cleveland.

THE PULSE RATE IN DIPHTHERIA DURING SLEEP. ALPHONS SOLÉ, Monatschr. f. Kinderh. **63**:380, 1935.

During the course of diphtheria the pulse rate may be normal and regular when the patient is awake and become irregular during sleep. Under such circumstances the patient should be watched with special care. While the symptom may be of no significance, but merely the result of nervous influences, it may be a sign of grave organic trouble. In the latter case, after a period of some days the irregularity is noticeable during the waking hours; in the former case it is not.

GERSTLEY, Chicago.

DIAGNOSIS OF RUBELLA. H. FLEISCHER, München. med. Wchnschr. **82**:1563 (Sept. 27) 1935.

Fleischer found the spleen palpable from 1 to 2 cm. below the costal margin in several cases of uncomplicated rubella which came under his observation. He believes that this diagnostic sign has been overlooked in rubella.

BRAHDY, Mount Vernon, N. Y.

ALLERGY IN DIPHTHERIA. JOSEF SIEGL, Wien. klin. Wchnschr. **48**:1127 (Sept. 13) 1935.

Siegl states that antitoxin dominates the picture of immunity to diphtheria, and many are inclined to regard such immunity as purely antitoxic in character. Various observations, however, point to the probability that the immunologic processes are not alone bound up with the formation of antitoxin. The observations of Hamburger and Siegl concerning the immunobiologic processes in children who spontaneously recovered from diphtheria without the aid of the antitoxin threw new light on this question. Among twenty such children, fifteen showed no provable amounts of antitoxin in the blood after they had been cured. These investigations indicate that antitoxin is not necessarily formed in the fight against diphtheria bacilli. Siegl believes that the existence of a specific allergy which leads to general resistance of the human organism to diphtheria can no longer be doubted. at any rate, the mechanism of immunity to diphtheria is more complex than has previously been supposed.

ABT, Chicago.

TREATMENT OF DYSENTERY WITH EXTRACT OF THE POSTERIOR LOBE OF THE HYPOPHYSIS. J. BARAL-SZABÓ, Orvosi hetil. **79**:382 (April 6) 1935.

The posterior lobe of the hypophysis diminishes inflammation of the colon and influences favorably its mobility. The latter influence is manifested on the ileum also.

The author used a posterior pituitary extract, which was given from two to five times daily. This extract was given to eight infants and ten children suffering from dysentery. This preparation was used only in severe cases. Fifteen of the eighteen patients had an elevated temperature, and four died. The author states that he is satisfied with the therapeutic effect of this treatment.

GÖTTCHE, Budapest, Hungary.

BACILLARY DYSENTERY IN EGYPT. M. ALI, J. Egyptian M. A. **18**:9 (Sept.) 1935.

After a comprehensive review of the literature on enteric infections in Egypt, Ali adds reports of seventy cases of patients with dysenteric symptoms who were studied bacteriologically during the spring and summer of 1932. Bacillary infections accounted for 82 per cent of the cases (the Flexner type, 34.3 per cent: the Shiga type, 10 per cent, and the Morgan type, 18.65 per cent); Endamoeba histolytica for 7.1 per cent, and unknown causes for 10 per cent. Inagglutinable strains of Bacillus dysenteriae Shiga and Bacillus dysenteriae Flexner were sometimes found, and special study was required to determine their relationship to the illness and to agglutinable strains.

MULHERIN, Augusta, Ga.

STUDIES ON SCARLET FEVER TOXIN: III. PURIFICATION OF SCARLET FEVER TOXIN AND ANATOXIN; TOXIN PRODUCTION OF SCARLET FEVER STREPTOCOCCUS IN SEMI-SYNTHETIC MEDIA. S. NAGATA, J. Orient. Med. **23**:13 (Aug.) 1935.

Methods of purifying scarlet fever toxin and anatoxin by zinc carbonate and zinc acetate are described. The toxicity and antigenicity of the preparations purified by these methods have been shown by the rabbit ear skin method.

Potent toxin produced in mediums of a semisynthetic type has been shown to be easily detoxified by solution of formaldehyde and heat, and it has been demonstrated that the anatoxin thus obtained possesses antigenicity.

EDITOR'S SUMMARY.

Acute Infectious Diseases

A COMPARATIVE STUDY OF THE GEOGRAPHIC DISTRIBUTION OF RHEUMATIC FEVER, SCARLET FEVER AND ACUTE GLOMERULONEPHRITIS IN NORTH AMERICA. DAVID SEEGAL, EMILY CARRIER SEEGAL and ELIZABETH L. JOST, Am. J. M. Sc. **190**: 383 (Sept.) 1935.

The absence of a decrease in the frequency of acute glomerulonephritis in southern latitudes might be interpreted as support of the hypothesis that agents other than the hemolytic streptococcus play the chief etiologic rôle in this disease. This does not seem likely, however, since considerable evidence is available incriminating the hemolytic streptococcus as the main incitant of the disease.

HENSKE, Omaha.

SYSTEMIC THRUSH IN CHILDHOOD. F. W. SCHLUTZ, J. A. M. A. **105**:650 (Aug. 31) 1935.

Thrush, one of the mycoses, is not caused solely by one species of fungus, Monilia albicans, but may be caused by a number of fungi. They belong to the large group of thallophytes, chlorophyll-free plant organisms which do not require carbon dioxide and are saprophytic or parasitic. There are two principal clinical types: the common white or gray-white and the more rare yellow or yellow-brown type. Thrush is not contagious, occurring only when conditions are favorable for its development. It generally remains localized, but it may involve the skin and internal organs extensively and invade the blood stream, giving rise to manifestations of generalized sepsis. A few cases of the latter type have been described. Four cases of generalized systemic thrush are reported in this article, and the author mentions another instance reported in a previous communication. In two cases dwarfing resulted, and in three alopecia developed. The fact that three patients died and the condition of the fourth is not improved indicates the formidable nature of the disease and the ineffectiveness of treatment.

BONAR, Salt Lake City.

ROCKY MOUNTAIN SPOTTED FEVER: RESULTS OF TEN YEARS' PROPHYLACTIC VACCINATION. R. R. PARKER, J. Infect. Dis. **57**:78 (July-Aug.) 1935.

Parker reports on ten years' use of the Rocky Mountain spotted fever vaccine and concludes that it has definite value, children being better protected than adults. The length of time that protection lasts is not known. Therefore, the vaccine is given each year.

TOOMEY, Cleveland.

THE USE OF THE ROENTGEN RAY IN INFECTIONS. RALPH E. MYERS, South. M. J. **28**:814 (Sept.) 1935.

If one judges from the reports of beneficial and oftentimes curative results in a wide range of acute and chronic inflammatory conditions, one must conclude that radiation therapy is worthy of consideration as an aid in the treatment of the majority of infectious processes.

Occasionally, radiation therapy seems to lower the resistance of the tissues to infection. This usually occurs when heavy radiation is used incident to the treatment of malignant disease. In many cases a fairly heavy radiation seems to exert a decidedly beneficial effect on infection.

There seems to be a rather common agreement among roentgenologists that only a moderate dose should be used. In different hands this may vary from 15 to 50 per cent of a skin erythema dose (300 r) but is rarely higher. The author records the use of from 15 to 25 per cent of a skin erythema dose and recommends even a somewhat smaller dose in children. The author also uses some filtration with copper instead of an aluminum filter alone. The filtration and voltage should be varied in accordance with the depth of the area to be treated. The treatments should generally be given from about seven to ten days apart. The author believes that, on the average, from three to four treatments may be required.

SCHLUTZ, Chicago.

RHEUMATISM AND ITS RESULTS. K. DOUGLAS WILKINSON, Lancet **2**:411 (Aug. 24) 1935.

In this comprehensive article rheumatic fever is considered from the historic, bacteriologic, clinical and therapeutic aspects.

In regard to the causative agent, the author states that the bacteriologic findings and the various experiments with toxins and antibodies all point to streptococcic infection as a predisposing cause. It is certain that the organism is not pyogenic; it is probable that it is nonhemolytic, and it may be that it is a saprophyte, harmless under normal conditions, which becomes virulent under special circumstances. These circumstances are not yet perfectly understood. Rest, removal of the foci of infection and the use of salicylates are the three essentials of treatment.

LANGMANN, New York.

RHEUMATIC HEART DISEASE AND VITAMIN C. C. BRUCE PERRY, Lancet **2**:426 (Aug. 24) 1935.

Rinehart and Mettier, in 1933, suggested that rheumatic fever may be the result of the combined influence of scurvy and infection. Since the capillary resistance test is not considered to be a criterion of vitamin C deficiency, the author studied five cases of active and six cases of quiescent rheumatic heart disease, with observation of the excretion of cevitamic acid in the urine after the administration of a test dose of vitamin C.

In three of the five cases of active disease a marked increase in the excretion of cevitamic acid following the test dose was shown, and the same result was obtained in three of the cases of quiescent disease.

The author agrees with Faulkner that any infection may increase the demand for vitamin C and secondary deficiency may develop, but that deficiency of vitamin C is not an important factor in the etiology of rheumatic fever.

LANGMANN, New York.

PREVENTIVE VACCINATION AGAINST SEASONAL GRIP IN CHILDREN. HENRI STÉVENIN and R. M. PATEZ, Arch. de méd. d. enf. **38**:322 (June) 1935.

In the agenda of the Third Conference of the International Association of Preventive Pediatrics, which convened at Luxemburg in September 1933, there were two contributions on influenzal vaccination. Frontal of Padua presented a favorable report on this procedure, while Rott of Berlin expressed the opinion that preventive inoculations of whatever nature are of extremely limited usefulness.

The authors report in considerable detail their experience in prophylaxis over a ten year period, especially in nurseries, where with the change of season, epidemics of grip are prone to develop and spread, in spite of the usual measures, such as the interdiction of nurses or attendants suffering from colds and the employment of masks. Encouraged by reports of successful vaccination against pneumonia among the Negro miners of South Africa and profiting by the assistance of the Pasteur Institute, Legroux and Bezançon, who had prepared a

vaccine which they used in the pandemic of 1918, gave this to twenty infants, who were later dispersed through groups in which grippal invasions were reported, but who remained well.

This observation was repeated at Lyon by Chatin and in other centers by Samsöen and Dreyfus, by Ribadeau-Dumas and Chabrun, and by D'Heucquerville of Boulogne, who utilized this method in several hundred cases.

In addition to the children in crowded wards, many persons in private practice were vaccinated, with the same favorable results, the organisms ordinarily cultured being the pneumococcus, various strains of the streptococcus, the bacillus of Pfeiffer and Micrococcus catarrhalis. Numerous histories of cases are cited in support of the authors' contentions.

AMESSE, Denver.

ACUTE TETANUS IN A CHILD OF THREE YEARS RAPIDLY CURED BY ANTITETANIC SEROTHERAPY ASSOCIATED WITH CHLOROFORM ANESTHESIA. M. LEREBOULLET, F. SAINT-GIRONS and J. ODINET, Bull. Soc. de pédiat. de Paris **33**:52 (Jan.) 1935.

A boy, 3 years old, had tetanus for which no portal of entry could be found. Antitetanic serum was administered subcutaneously, intramuscularly and intraspinally, in the latter case under chloroform anesthesia. Treatment was begun on the third day of the disease, and a total of 420 cc. of antitetanic serum, representing 20,000 units, was given, 100 cc. of which was injected intraspinally during six lumbar punctures. Chloroform anesthesia was administered nine times for periods not exceeding from twenty to twenty-five minutes, and the amount inhaled was progressively decreased from 15 to 5 cc. The child recovered.

BENJAMIN, Montreal, Canada.

KALA-AZAR. M. D'ŒLSNITZ, Nourrisson **23**:303 (Sept.) 1935.

Kala-azar has been endemic in southern France since the beginning of the present century. Cases are encountered in both adults and infants. In diagnosis the important triad is fever, anemia and splenomegaly. Various other diagnostic procedures, including splenic puncture, are described and discussed. In the differential diagnosis other common causes of splenomegaly (malaria, infection due to Brucella melitensis, tuberculosis and syphilis) must be considered. The most valuable drug in the treatment of kala-azar is antimony.

MCCLELLAND, Cleveland.

POLYARTICULAR GONOCOCCIC PSEUDORHEUMATISM. ROBERTO INFANTE Y., Arch. Hosp. de Niños, Roberto del Rio **4**:15 (March) 1933.

The author describes this condition in a girl, 6 years old, ill with pertussis. The symptoms in the joints appeared fifteen days after the development of the disease. Various joints, such as those of the shoulder, wrist and phalanges, were involved and showed intense acute inflammation. A purulent urethral discharge showed large numbers of gonococci and explained the etiology of this unusual complication.

SCHLUTZ, Chicago.

OCCURRENCE OF BACILLUS SUIPESTIFER IN A CASE OF INFECTION IN A CHILD. L. KUN and P. SVASTITS, Orvosi hetil. **79**:827 (July 27) 1935.

The right shoulder joint of an infant, aged 4 months, became swollen and painful. Aspiration resulted in the withdrawal of 5 cc. of greenish-yellow pus. Arthrotomy was performed, and recovery was prompt. On the first bacteriologic examination influenza bacilli were observed. On the second examination bacillus suipestifer was isolated, but the influenza bacillus was not observed. The serum of the infant agglutinated B. suipestifer in a dilution of 1:3,200. B. suipestifer was not observed in the feces. The mother of this infant was a vagrant gypsy.

who often ate diseased pork. Her serum did not agglutinate B. suipestifer. The child at first had an influenzal infection, which attacked the shoulder joint and in some way prepared it for the secondary invasion of B. suipestifer from the gastro-intestinal tract. GÖTTCHE, Budapest, Hungary.

INFECTIVE RETICULO-ENDOTHELIOSIS WITH SPECIAL LOCALIZATION IN THE LUNGS, BONE MARROW AND THYMUS. S. VAN CREVELD and F. H. TER POORTEN, Nederl. tijdschr. v. geneesk. **79**:3947 (Aug. 17) 1935.

The clinical and pathologic observations are reported in a case of reticulo-endotheliosis occurring in a girl of 4 months. It was assumed that an infection was the cause of the proliferation of the reticulo-endothelial system. Clinically, general cystic osteitis (extensive skeletal lesions) and the development of a map like skull were prominent. Pathologically, moreover, a special localization of the process was observed in the thymus and lungs, the latter organs showing even macroscopically a peculiar picture. The clinical symptoms and the abnormalities observed at autopsy are compared with those noted in a number of analogous cases recorded in recent years. The differential diagnosis from well known forms of reticulo-endotheliosis is stressed. AUTHORS' SUMMARY.

Chronic Infectious Diseases

CONGENITAL SYPHILIS IN CHILDREN: I. FRANK R. SMITH JR., Am. J. Syph. & Neurol. **19**:532 (Oct.) 1935.

The author's summary is as follows:

"1. The results of treatment in 279 patients with early congenital syphilis are analyzed. These were followed for a minimal period of two years with a mean of 6.2 years.

"2. Congenital syphilis is a material factor in the cause of death in children under six months of age, decreasing rapidly after that time.

"3. The beneficial results of prenatal treatment upon the child are in direct proportion to the amount of treatment given the mother. The incidence of lesions in the children, of Wassermann-fastness, and the 'ultimate clinical outcome' are all affected by it. Prenatal treatment may not only prevent the infection in the fetus but, if infection does occur, may serve as early treatment in utero."

ROYSTER, University, Va.

THE DIAGNOSIS OF INFANTILE CONGENITAL SYPHILIS DURING THE PERIOD OF DOUBT. NORMAN R. INGRAHAM JR., Am. J. Syph. & Neurol. **19**:547 (Oct.) 1935.

To be fully appreciated, this article must be read in the original. A review of some of the literature is given, with an outline of the materials used. Ingraham's method of procedure in establishing the diagnosis of syphilis is then described: First, a careful search for syphilis in the mother should be made. Then the effects of the duration of the disease in the mother and of prepartum treatment as to the presence or absence of the disease in the child should be determined. Physical examination of the infant is stressed. The diagnosis should be based on the Wassermann reaction, the sedimentation rate of the blood and positive findings on dark-field examination of the umbilical vein. Roentgenographic studies of the long bones are of the greatest importance. It is emphasized that no infant who is suspected of having contracted syphilis in utero from the mother should be treated for this disease until it is proved to have it. ROYSTER, University, Va.

MERCURY INUNCTIONS. TORALD SOLLMANN, H. N. COLE and N. E. SCHREIBER, Arch. Dermat. & Syph. **32**:242 (Aug.) 1935.

The first portion of the paper is devoted to the influence of the vehicle on the absorption of mercury. Several different bases were used in these experiments,

and the method of preparing each is carefully given. A second portion of the paper is devoted to inunctions with mercury oleate ointments. The formulas for the several ointments are included. The result of the absorption of mercury is expressed in the urinary excretion of the metal in each of the experiments. The advantages of the oleate ointments are their cleanliness, the lack of detection by telltale stains and the far greater ease of inunction. The authors believe that these advantages show a definite therapeutic advance. Next, inunctions with colloidal mercury ointments are discussed. The authors found the absorption of mercury from such ointments to be "generally very poor." A concluding review of studies of mercurial inunctions is included. The advantage of the oleate is mentioned. That and the 50 per cent ointment of metallic mercury are the most effective forms. The ointment vehicles are unimportant from the standpoint of efficiency but should be sufficiently stiff to prevent settling of the mercury. The removal of the excess ointment by benzene diminishes the amount of mercury absorbed. Massive inunctions with the 30 per cent ointment are fully effective. DULIN, Iowa City.

ENLARGEMENT OF ONE STERNOCLAVICULAR ARTICULATION AS A VALUABLE CLINICAL SIGN OF LATE PRENATAL (CONGENITAL) SYPHILIS. MAURICE DORNE and SAMUEL J. ZAKON, Arch. Dermat. & Syph. **32**:602 (Oct.) 1935.

"In 1930 Higoumenakis described as a new sign of late prenatal syphilis, the enlargement and anteroposterior thickening of the sternal end of the clavicle." The enlargement is unilateral and on the right side, except in left-handed persons, in whom it occurs on the left side. The enlargement reaches a permanent stage at about the age of puberty. A photograph of a patient with this stigma is included. A table is given showing data for 12 patients with this sign and the comparative frequency of other stigmas. In Higoumenakis' original series of 23 cases, he found 7 patients with this stigma who had other signs of the disease, along with a positive Wassermann reaction, while 16 had a negative Wassermann reaction but had other signs of syphilis besides the clavicular enlargement. He found this sign in 170 of 197 cases; the next most common sign was rhagades, which was observed in 132 of 197 cases. The authors comment that the English literature fails to reveal any articles relative to this sign, although a few abstracts and a note by Stokes in his textbook were found. DULIN, Iowa City.

TUBERCULOSIS IN THE ADOLESCENT. D. S. BEACHMAN, J. Michigan M. Soc. **34**:534 (Sept.) 1935.

Beachman again stresses the importance of adolescence as the crucial period in pulmonary tuberculosis. His article deals with a case-finding experience in the eleventh and twelfth grades of high schools in Detroit. Of 8,015 tuberculin tests, 1,861 gave positive results. Thirty-four students who were examined roentgenographically showed the adult type of the infection, and 382 had the childhood type. The analysis of the 34 persons with the adult type of the disease (28 white and 10 colored) showed that the process was minimal in 82.1 per cent and moderately advanced in 17.9 per cent. None of the white group showed far advancement. In the 10 colored children the disease was minimal in 83 per cent, moderately advanced in 16.6 per cent and far advanced in none. A history of contact with a known case of tuberculosis was given in only 5 instances. In the author's summary attention is called to the fact that the onset of tuberculosis may be acute and that the disease begins to appear more frequently in adolescence. Overcrowding makes for the spread of the disease, and infection takes place more readily in the family or household. The roentgen rays are considered important in the diagnosis and treatment. CAREY, Detroit.

TUBERCULOUS CARIES OF VERTEBRAL BODIES. GEORGE G. ORNSTEIN, Quart. Bull., Sea View Hosp. **1**:3 (Oct.) 1935.

It has long been held that the diagnosis of tuberculous disease of the spine rests on the presence of pain, stiffness, weakness, awkwardness and deformity. In addition to these, roentgen evidence of osseous destruction is usually considered necessary. Ornstein points out, however, that these are in most instances the characteristics of a late stage of the disease and that all may be absent and yet a diagnosis be possible. The presence of paravertebral abscess is the earliest detectable sign of spinal caries and may be present long before any bony changes are evident on roentgen examination or any symptoms complained of. Recognition of such early signs of disease requires an accurate roentgen technic. The use of the fluoroscope to visualize the posterior mediastinum, with the patient rotated, is an important aid. An anteroposterior view may visualize the abscess, which is then nearer the film, better than an postero-anterior view. Any doubtful shadow in the mediastinum and any slight abnormal widening or irregularity should be viewed with suspicion.

It is important also to bear in mind that the pus from carious areas may burrow its way to most unusual localities. It may discharge into the pleural or peritoneal spaces, resulting in tuberculous pleurisy or peritonitis. In other cases it follows the ribs around the thorax and may discharge in the region of the sternum. A discharging sinus in the neck may be mistaken for a suppurating gland. Fluoroscopic examination following the injection of iodized poppy-seed oil 40 per cent, if this is successfully carried out, will reveal the true origin of the discharge.

A number of reports of cases are cited to verify the author's thesis.

EUGENE SMITH, Ogden, Utah.

USE OF INSULIN IN NON-DIABETIC TUBERCULOUS CHILDREN. HAROLD ROSENBERG and CAMILLE KERESZTURI, Quart. Bull., Sea View Hosp. **1**:76 (Oct.) 1935.

By the use of insulin an acceleration of the rate of gain in weight was obtained in fifteen of seventeen nondiabetic children. Of these fifteen, thirteen children maintained the gain after the insulin was discontinued. The follow-up period in most cases was three months. After the fourth week the weight gained was too small to warrant the use of insulin for a longer period. The subjective reaction of the children to insulin is no criterion of its efficacy.

EUGENE SMITH, Ogden, Utah.

ROUTINE TUBERCULIN TESTS IN CHILDREN. C. V. RICE, South. M. J. **28**:942 (Oct.) 1935.

Rice believes that a positive tuberculin reaction with a purified protein derivative indicates that tuberculous infection has taken place.

In a child aged from 2 to 5 years with a positive reaction and with persistent symptoms it is suggestive that these symptoms are tuberculous in origin.

In infants a positive reaction has clinical value, and tuberculosis is more progressive than in older children and generally leads to a fatal outcome.

The younger the child the worse the prognosis. Therefore, tuberculin tests should be used in all routine examinations of infants and of preschool and grade school children. This practice will lessen the contacts, reduce the mortality and aid in stamping out tuberculosis.

SCHLUTZ, Chicago.

CONGENITAL SYPHILIS AND SPLENIC ANEMIA IN AN INFANT. HUGH THURSFIELD, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **27**:1319 (Aug.) 1934.

A patient aged 2 years had been treated for congenital syphilis with a suspension of bismuth oxychloride. On admission to the hospital the Wassermann

reaction was negative. The child had jaundice. The liver and spleen were much enlarged. The blood count was as follows: red cells 1,800,000 per cubic millimeter, hemoglobin 35 per cent, color index 0.96, white cells 6,300 per cubic millimeter, reticulocytes 3.7 per cent, normoblasts 2 per cent, myeloblasts 1 per cent, myelocytes 1 per cent, polymorphonuclears 39 per cent, lymphocytes 50 per cent, mononuclears 6 per cent and eosinophils 3 per cent. The reaction to the indirect van den Bergh test was positive in one unit. The patient suffered from mild pyrexia of an irregular type. Three months later, after a transfusion, splenectomy was performed. After operation there was a brisk outpouring of nucleated red cells into the circulation. A complete hematologic chart giving the details in the case and a photograph of the child accompany the report. WILLIAMSON, New Orleans.

THE PREVENTION OF TUBERCULOSIS IN CHILDHOOD BY METHODS OF SEPARATION. G. GREGORY KAYNE, Tubercle **16**:433 (July); 494 (Aug.) 1935; **17**:10 (Oct.) 1935.

Kayne presents the results of his observations on the method for the prevention of tuberculosis in childhood by separation of children from infected households, as practiced especially in France and Belgium. In the former country the usual practice is to board out the children in selected rural families under careful nursing and medical supervision. In Belgium the child is given institutional care during separation. The details of both methods are fully elaborated, and the statistical results of such care are analyzed. EUGENE SMITH, Ogden, Utah.

IDIOSYNCRASY TO SULFARSPHENAMINE. EARLY AND SEVERE REACTION IN A GIRL EIGHTEEN MONTHS OLD AFTER AN INTRAMUSCULAR INJECTION OF 0.03 GM. OGLIASTRI and SIDI, Bull. Soc. de pédiat. de Paris **32**:624 (Dec.) 1934.

Immediately after an intramuscular injection of sulfarsphenamine (0.03 Gm.) a nitritoid reaction occurred in a girl 18 months old, who was suspected of having congenital syphilis. This was the third injection of a second series, as she had been given a first course of treatment totaling 0.68 Gm. about three months previously, without any reaction. She presented the picture of collapse with extreme cyanosis. Half a milligram of epinephrine hydrochloride was injected hypodermically, and the child recovered. She had a purpuric eruption on both hands and forearms, which disappeared after five days. Nitritoid reactions are observed more frequently after intravenous injections, but they do occur, although rarely, after intramuscular and even subcutaneous injections.

BENJAMIN, Montreal, Canada.

FAMILIAL HEREDITARY SYPHILIS. L. BABONNEIX, Bull. Soc. de pédiat. de Paris **33**:28 (Jan.) 1935.

A girl, 7 years old, presented hepatomegaly, frontal prominences and dental lesions suggestive of hereditary syphilis. Her younger sister had none of the common characteristic signs of the disease, but because of a highly arched palate, absence of the xiphoid process, internal strabismus and slight irregularity of the pupils she was considered as probably afflicted with the disease. The mother had small and widely spaced teeth and was also considered as probably having hereditary syphilis. The Wassermann reaction of her blood, as well as the Wassermann reaction of the father's blood, was negative. No mention is made of the results of the serologic tests on the children. If the children and the mother had syphilis, the condition in the former would illustrate the hereditary form of this disease in the second generation.

BENJAMIN, Montreal, Canada.

WHAT THE PHYSICIAN SHOULD KNOW ABOUT BCG. LÉON TIXIER, Bull. Soc. de pédiat. de Paris **33**:65 (Jan.) 1935.

BCG has not been proved to be successful in vaccination against tuberculosis. It is pointed out that a person who is afflicted with the disease and recovers when it is arrested is by no means immune to it but, on the contrary, is more susceptible to further infection; this argues strongly against the possibility of vaccination against it by the administration of bacilli. That the general resistance of young children who have been vaccinated against infection with BCG is better than that of those who have not has been reported by Calmette and others, but the author contradicts this conclusion as a result of his experience in his own practice. He does not agree that the administration of BCG is without danger, and as untoward sequelae cannot be foreseen he is not in favor of giving it to infants in a healthy environment. He inveighs vehemently against the definite opinion in favor of it which the French press publishes, when it is impossible for physicians to do so in the light of present impartial and accurate observation, as was reported by the section on hygiene of the League of Nations.

BENJAMIN, Montreal, Canada.

TREATMENT OF EXTERNAL TUBERCULOSIS, PARTICULARLY OF TUBERCULOUS CERVICAL ADENITIS. R. BLOCH and R. MICHAUT, J. de méd. de Paris **54**:805 (Sept. 20) 1934.

Eighty-nine patients were treated exclusively with injections of a specially prepared bacillary extract. Sixty-nine per cent of these had tuberculous cervical adenitis; the others had tuberculous fistula of the bone, cold abscess, synovitis or tuberculous salpingitis. Thirty-three patients were cured, and thirty were definitely improved; the others did not persist in treatment.

Six other articles in this journal report good results in similar cases with the use of this extract.

LESLIE, Evanston, Ill.

ACQUIRED SYPHILIS IN THE INFANT AND CHILD. H. GRENET, Paris méd. **2**:371 (Nov. 2) 1935.

Grenet agrees with M. Péhu that in at least 3 or 4 per cent of the cases of syphilis in infants and children the disease is acquired. In the major portion of these cases infection is accidental rather than venereal. Accounts of various cases in which the disease was due to accidental infection are given.

LESLIE, Evanston, Ill.

PROTEINEMIA IN TUBERCULOSIS IN CHILDREN. A. FIANO, Riv. di clin. pediat. **33**: 897 (Aug.) 1935.

The protein content of the blood serum of sixty-seven children was determined by the refractometer. Of these children, thirty-six had hilar tuberculosis; twenty, active parenchymal tuberculosis of the lungs; seven, pleurisy with effusion; two, tuberculous meningitis, and two, erythema nodosum. The protein content of the blood serum was normal in the great majority of cases of hilar tuberculosis; in four of the thirty-six cases it was above normal. In the cases of active tuberculosis normal values were also obtained, except in two cases of severe parenchymal pulmonary tuberculosis, in which there was hypoproteinemia. In the cases of erythema nodosum and of tuberculous meningitis the protein of the blood serum was normal. In the cases of tuberculous pleurisy with effusion there was a lowering of the blood protein content while there was active effusion; the blood protein content rose to normal when the fluid had been reabsorbed. The blood protein content seemed to run parallel with the hemoglobin content; that is, a high blood protein level accompanied a high hemoglobin level and a low blood protein level accompanied a low hemoglobin level. A relation between proteinemia and the red blood count was not so apparent.

HIGGINS, Boston.

TUBERCULOSIS IN INFANTS. A. FIANO, Riv. di clin. pediat. **33**:997 (Sept.) 1935.

Fiano reports twenty cases of tuberculosis in children under 2 years of age, several of whom were followed over a period of from three to five years. The children did remarkably well and frequently showed definite improvement (or cure), which was confirmed by roentgen examination. The author feels that the prognosis for the infant with tuberculosis is usually favorable.

HIGGINS, Boston.

EARLY DIAGNOSIS OF POTT'S DISEASE. A. RODRÍGUEZ CASTRO, Arch. de pediat. d. Uruguay **6**:361 (Aug.) 1935.

The author reports the case of a boy 11 years old in whom the diagnosis of Pott's disease was established in spite of the fact that roentgenography showed no manifest lesions in the vertebral column. He agrees with many other observers that negative roentgenologic findings are not significant in the early stages of Pott's disease.

SCHLUTZ, Chicago.

PROPHYLAXIS OF TUBERCULOSIS IN CHILDHOOD. ALVARO SILVA, Bol. Soc. cubana de pediat. **7**:85 (Feb.-March) 1935.

Since tuberculosis is a contagious disease which primarily affects young children, the principal effort should be directed to the most complete protection of persons of this age group against the disease. There is no specific treatment for the disease; prophylaxis is therefore the most promising measure of protection.

The care of children of tuberculous parents in colonies, after the model of the noted French pediatrician Grancher, has been successful in reducing the morbidity in tuberculosis from 60 to 0.3 per cent and the mortality from 40 to 0.1 per cent.

The author unqualifiedly recommends generalized immunization with the BCG vaccine and considers it one of the most effective measures against tuberculosis.

SCHLUTZ, Chicago.

TREATMENT OF CONGENITAL SYPHILIS IN THE YOUNG INFANT WITH ACETARSONE. FEDERICO EGGERS, Rev. chilena de pediat. **5**:492 (Sept.) 1934.

The drug acetarsone contains 27.3 per cent arsenic. It can be given in the form of tablets. Each tablet contains 0.25 Gm. of the drug and 0.07 Gm. of arsenic.

The author considers acetarsone to be the drug of choice for treatment of the infant up to the age of 2 years. It has the advantage of oral administration.

Acetarsone is usually given in seven treatments of ten days each for a total period of seventy days, followed by a period of rest, and then a second course of five treatments of four days each, or a total of twenty days, is carried out. In about 50 per cent of the cases a second series of treatments is required. No untoward symptoms result from the use of the remedy.

SCHLUTZ, Chicago.

VASCULAR SYPHILIS WITH LATE MANIFESTATIONS OF HEREDITARY SYPHILIS. MARCO MALDONADO A., Rev. chilena de pediat. **6**:201 (May) 1935.

A congenitally syphilitic boy, 11 years old, presented aortic insufficiency complicated with an aneurysm of the left carotid artery. The author discusses three possibilities of treatment of the aneurysm, namely, ligature, extirpation and incision, and points out the dangers of each of these procedures.

SCHLUTZ, Chicago.

RÔLE OF THE CAPILLARY FUNCTION IN DETERMINING THE RESULT OF THE PIRQUET REACTION. R. SUNKEL, Dermat. Wchnschr. **100**:361 (March 30) 1935.

An ointment containing acetylcholine was found to cause local active hyperemia. In thirty-two patients with various grades of acrocyanosis this ointment was rubbed into an area of one arm for five minutes, and the ointment base was rubbed into the other arm for the same period. An hour later a Pirquet test was performed on each arm. Seven patients gave no reaction on either arm; one showed an equal reaction on both arms, and the remaining twenty-four showed a weaker reaction or no reaction at all on the control area. Sunkel concludes that this is evidence that a positive Pirquet reaction is more likely to occur in the presence of increased capillary activity.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

OSMOTIC REGULATION IN TUBERCULOUS MENINGITIS. DENES VON MORITZ, Monatschr. f. Kinderh. **63**:245, 1935.

In twelve cases of tuberculous meningitis the albumin content of the blood serum was slightly increased, and the freezing point was raised. This hyposmosis follows a diminution of the fixed base content and the chloride content. As the base content and the chloride content are both diminished, one should speak of hyposalemia rather than of isolated hypochloremia. The disturbance of the salt metabolism is probably of central origin.

GERSTLEY, Chicago.

PROPHYLAXIS OF TUBERCULOSIS IN CHILDREN. J. KRAMÁR, Orvosi hetil. **79**:743 (July 6) 1935.

Infection of infants and young children with tuberculosis should be prevented in every way. This is easy in healthy families. Children in an infected family should be isolated and vaccinated with BCG. Prophylaxis in kindergartens and other schools is a problem for the school physician. Children with slight infections should be sent to open-air schools or to school sanatoriums.

GÖTTCHE, Budapest, Hungary.

COMPARATIVE DIAGNOSTIC VALUE OF CHANGES IN THE EYE IN CONGENITAL SYPHILIS OF EARLY CHILDHOOD. V. V. CHIRKOVSKIY and E. I. RAUTENSHTEYN, Sovet. vestnik oftal. **7**:289, 1935.

This is a serious and thorough study of the diseases of the eye in children with congenital syphilis. The changes in the choroid and retina, the optic nerve, the iris and the conjunctiva are discussed in detail. A wide literary review is given; six tables illustrate the paper.

The material consisted of 231 children who suffered from congenital syphilis and who were observed for a period of five years (1929-1934) in the syphilogic clinic of the Leningrad Institute for Protection of the Health of Mothers and Infants. The ages of 106 of the children ranged up to 3 months, and those of 78, from 3 months to 1 year; i. e., 79.6 per cent were aged up to 1 year; the other 47 children were from 1 to 5 years old.

One group of the children (91) suffered from florid syphilis and the rest (140, or 60.6 per cent) from latent syphilis. The most frequent changes observed were those of chorioretinitis, type 1, after Sidler, in either a mild or a marked form. The spotted appearance of the fundus was typical for both forms; this was due to small, light, round, reddish yellow pigmented spots, or so-called "pepper and salt" retinitis. These changes were observed in 40 children, or in 17.3 per cent; 31 were affected before the age of 6 months. In 22 of these the chorioretinal changes were mild. Of 11 children who had a negative Wassermann reaction of the blood, 5 showed chorioretinitis as the only decisive sign for the diagnosis of congenital syphilis. The histopathologic changes occurred in the choriocapillary

layer of the choroid and in the pigmented epithelium of the retina. The dark spots were epithelial cells crowded with pigment and the light spots those containing little or no pigment. Type 2 retinitis after Sidler (large round or oval pigmented spots in the periphery of the fundus) was met with in only 2 patients, 2 and 5 years old.

Changes in the optic nerve alone were observed by the authors only in 7 cases, 5 of florid and 2 of latent syphilis. There were 5 instances of optic neuritis and 2 of postneuritic optic atrophy. In 5 of these neuritis occurred within the first three months after birth. In all these cases there was severe generalized syphilis, and the syphilis of the mothers was of long standing.

Iritis was observed in 3 children only; the youngest was 48 days old. One of these patients had changes also in the choroid. The mother contracted syphilis in the latter part of her pregnancy.

One case of parenchymatous keratitis was seen in a child aged 6 weeks; it died soon from hemolytic icterus and visceral syphilis. In one case of peculiar conjunctivitis with thickening of the conjunctiva and small spots at the fornix the condition was doubtless syphilitic. The child was 5 months old and had papules on the skin.

The authors' conclusions are:

1. The most frequent disease of the eye in congenital syphilis is chorioretinitis, type 1, after Sidler.

2. Type 1 retinitis was observed in 40, or 17.3 per cent, of 231 children.

3. The marked as well as the mild forms of "pepper and salt" chorioretinitis type 1 have definite diagnostic value.

4. The mild forms of chorioretinitis without pigmentation are the initial changes from which "pepper and salt" retinitis gradually develops.

5. The comparative diagnostic value is particularly high in the latent forms of syphilis, as in 11 of 20 cases the changes in the fundus were the only diagnostic signs.

6. The ophthalmoscopic examination is important also in manifest syphilis, as the changes in the fundus appear very early in congenital syphilis.

7. Optic neuritis and optic atrophy are rare in congenital syphilis.

8. Iritis is rare in congenital syphilis, as only 3 cases of iritis were seen; all the patients suffered from severe generalized syphilis.

9. Examination of the conjunctiva should be included, as in rare instances specific conjunctivitis may be observed (1 case).

10. The majority of the ocular involvements were observed in children whose mothers received little or no antisyphilitic treatment.

11. The general conclusion is that systematic examination of the eyes of syphilitic children is important, particularly at an early age.

SITCHEVSKA, New York. [ARCH. OPHTH.]

MILIARY TUBERCULOSIS IN EARLY CHILDHOOD. C. B. RODKIN and P. C. KLIMENKO, Vrach. delo **18**:23, 1935.

Rodkin and Klimenko present a detailed account of the symptomatology and clinical types of miliary tuberculosis in young children, together with some reports of cases illustrating the various forms of the disease. The clinical material consisted of thirty-five patients, twenty-two of whom were under 1 year of age; the rest were between 1 and 3 years of age.

The authors' conclusions were as follows:

1. The view formerly held that miliary tuberculosis in young children always runs an acute and fatal course needs to be revised.

2. The clinical picture and symptomatology of miliary tuberculosis is too varied to permit an accurate classification.

3. Dyspnea, cyanosis and splenomegaly are not pathognomonic of miliary tuberculosis in young children, and therefore neither their presence nor their absence can serve as a definite criterion in the diagnosis of the disease.

4. The early diagnosis of miliary tuberculosis is considerably aided by the roentgen rays.

5. A regimen of general hygienic and dietary measures when instituted early may sometimes save the patient. This is especially true in the localized forms of the disease, in which one isolated organ is affected (chiefly the lungs) and which are so frequently met with in young children. BODER, Los Angeles.

Diseases of Blood, Heart and Blood Vessels, and Spleen

BIOPSY OF THE STERNAL BONE MARROW: ITS VALUE IN THE STUDY OF DISEASES OF BLOOD-FORMING ORGANS. WILLIAM DAMESHEK, Am. J. M. Sc. **190**:617 (Nov.) 1935.

The blood picture is the end-result of many complex factors which have to do with the growth, destruction and liberation of the blood cells from the various hematopoietic organs. Identical blood pictures may be associated with fundamentally different disorders. The bone marrow, as the chief blood-forming organ, must deserve the greatest consideration, since most of the so-called blood diseases either originate there or are associated with various abnormalities of growth within its confines.

Biopsy of the sternal bone marrow with a small trephine was performed in about one hundred and twenty-five cases of diseases of the blood-forming organs. The criteria for cellular diagnosis, together with the findings in the miscellaneous group of diseases, are briefly discussed and the diagnostic implications considered.

In many cases in which obscure anemia is present the condition cannot be readily diagnosed. Biopsy of the marrow has proved to be of greatest value in the diagnosis of these conditions. Particularly, it has demonstrated that many cases of so-called Banti's disease, splenic anemia, agranulocytosis, aplastic anemia and pernicious anemia are in reality instances of aleukemic leukosis. Anemia, leukopenia and thrombocytopenia are a triad of laboratory findings which point to a destructive ("myelophthisic") process in the marrow, which is usually leukemic in type. Cases illustrating the diagnostic value of biopsy of the bone marrow are briefly described. HENSKE, Omaha.

THE USE OF BACTERIOPHAGE AND CULTURE FILTRATES IN CHILDREN WITH CARDIAC DEFECTS. MARTIN M. MALINER and MARGARET E. STRAUB, Arch. Pediat. **52**:733 (Nov.) 1935.

In view of the fact that Streptococcus viridans is recognized as the etiologic agent in endocarditis lenta, the authors prepared a streptococcus phage and filtrate for experimental use in the prevention of this condition. Seventeen children selected for study received upward of twenty-three intravenous injections of phage and filtrate. No conclusions were arrived at. The hope is expressed that such a method may be helpful in the prevention of infection due to Streptococcus viridans. WADDELL JR., University, Va.

NUTRITIONAL ANEMIA. GEORGE E. ROBERTSON, Nebraska M. J. **20**:452 (Dec.) 1935.

Three cases of anemia in premature infants, two of them twins, are reported. The case of a full term baby who became intensely jaundiced shortly after birth,

whose hemoglobin content fell from 95 to 60 per cent and who was given 20 cc. of blood intramuscularly on two occasions and an intravenous injection of 65 cc., is also reported. Egg yolk, puréed vegetables and a mixture of cereals were administered early. In addition to the varied diet, medication consisted of the administration of iron and liver extract. Good results are reported.

HAMILTON, Omaha.

ATYPICAL MEGALOCYTIC ANAEMIA. G. D. KERSLEY, Brit. M. J. **2**:994 (Nov. 23) 1935.

Kersley reports five cases of a condition that falls under the classification of atypical megalocytic anemia. The summary is as follows:

"Five cases of atypical megalocytic anaemia are described. In the first, in a boy of 11, the stomach showed normal acidity and the condition reacted well to liver therapy.

"The second case demonstrated the development of a megalocytic from a microcytic anaemia in a woman with normal gastric acidity. The condition failed to react to liver or iron therapy until after blood transfusion. The condition was associated with tetany.

"Cases III and IV appeared typical of pernicious anaemia; in Case III the anaemia was associated with soreness of the tongue, but analysis of the gastric contents in both cases showed the presence of free hydrochloric acid."

ROYSTER, University, Va.

RAPIDLY FATAL AGRANULOCYTOSIS IN A CHILD OF FIVE YEARS. G. BLECHMANN and P. BAGOT, Bull. Soc. de pédiat. de Paris **32**:357 (June) 1934.

A girl, 5 years old, had infection of the throat accompanied with cervical adenitis. She presented marked leukopenia, with few polymorphonuclear neutrophilic leukocytes, and a considerable degree of anemia. Despite two transfusions she died of pneumonia thirteen days after the onset of the illness, though the temperature dropped and she was apparently improved on the seventh day. Cases of agranulocytosis in children have been reported with increasing frequency during the past few years, and it is pointed out that they are often accompanied with other evidence of blood dyscrasia, such as thrombocytopenia and purpura.

BENJAMIN, Montreal, Canada.

HEMOLYTIC ICTERUS TREATED WITH SPLENECTOMY. L. BABONNEIX and JOURDAN, Bull. Soc. de pédiat. de Paris **33**:24 (Jan.) 1935.

A boy, 11½ years old, was admitted to the hospital because of severe anemia. He had been subicteric during the past year, and became very pale, especially after illness due to any infection. Bilious vomiting was also frequent. There was marked enlargement of the spleen and liver. There was no definite jaundice, but the urine contained bile pigments, bile salts and traces of urobilin. The blood contained an abnormal amount of bilirubin. There was a slight increase in the fragility of the red cells. The red cell count was 746,660 per cubic millimeter. After the patient had received four blood transfusions and a diet high in liver content for over a month, marked improvement was shown in the general condition; the red cell count increased to over 3,000,000, and the spleen and liver diminished in size. Splenectomy was then performed, and the patient made an excellent recovery. About ten days after the operation he had gained weight; the color was good; the red cell count was over 4,000,000 per cubic millimeter, and the results of the fragility tests were almost normal.

BENJAMIN, Montreal, Canada.

Diseases of the Blood in 1935. P. Harvier and J. Bernard, Paris méd. **2**:197 (Sept. 21) 1935.

A review of the present knowledge regarding anemia, leukemia, Hodgkin's disease, agranulocytosis, infectious mononucleosis and the hemorrhagic diseases is given. There is also a brief discussion of blood transfusion and the blood groups. Numerous references are given.

Leslie, Evanston, Ill.

Splenic Puncture in Blood Diseases. S. Perlès, Paris méd. **2**:217 (Sept. 21) 1935.

The technic of splenic puncture is presented and its value in obscure cases of splenomegaly pointed out. A needle of a diameter of from 0.08 to 0.1 mm. is used. Following the application of a local anesthetic and the immobilization of the diaphragm in inspiration, rapid and forceful aspiration is carried out. The plunger is allowed to return to its position at rest, and the needle is withdrawn without further aspiration. Blood should not appear in the body of the syringe. The patient should be allowed at least twelve hours' rest following the procedure, with an ice-bag applied over the spleen. Plates illustrate smears of the normal splenic pulp and the findings in chronic lymphatic leukemia, acute lymphatic leukemia and myeloid leukemia.

Leslie, Evanston, Ill.

Size of the Erythrocytes in Healthy and Normal Children After the Fourth Year of Life. C. De Murtas, Riv. di clin. pediat. **33**:1045 (Sept.) 1935.

De Murtas used the apparatus of De Castro to measure the size of the red blood cells of thirty children between 4 and 12 years of age. He found that the red cells invariably measured between 6.2 and 9.3 microns in diameter. Within these limits are the normocytes, the normal microcytes and the normal macrocytes of the blood.

Higgins, Boston.

A Case of Arteriosclerosis in a Child with Malignant Nephrosclerosis. Frederico Patiño Mac-Iver, Arch. Hosp. de Niños, Roberto del Rio **5**:61 (June) 1935.

The author reports the exceedingly rare condition of arteriosclerosis associated with nephrosclerosis in a child 8 years old. The principal disorder was gradual loss of weight, with unusual fatigue, accompanied by severe headaches and frequent attacks of epistaxis. Occasionally there was severe transitory abdominal pain. Small tumor masses were felt in the abdomen, on the inner surfaces of the arms and over the base of the skull. The tumor masses seemed to follow the course of the deeper vessels and were attached to them. The spleen was very large. The blood pressure was elevated. Such arterial vessels as were palpable were hard and rigid. Both fundi showed neuroretinitis. The urine showed some blood and traces of albumin. The child showed the complete picture of hypertension. Biopsy of the tumor masses with the involved artery showed circumscribed obliterating endarteritis and periarteritis fibrosa. At autopsy generalized sclerosis of all vessels and particularly of those of the kidneys was noted.

Schlutz, Chicago.

Congenital Hemolytic Icterus. J. G. Cabrera Calderín, J. M. Labourdete Scull and Gervasio Prado, Bol. Soc. cubana de pediat. **7**:299 (Oct.) 1935.

The case of a girl 9 years old with congenital hemolytic icterus is reported. The icterus was moderate; there was urobilinuria but no acholic stool. Itching and bradycardia were absent. The spleen was large. The patient showed the characteristic blood picture of a moderate degree of secondary anemia, slight evidence

of regeneration of blood and increased cell fragility. Other members of the family showed some of the same symptoms.

Splenectomy is usually the treatment of choice in this condition, but it does not always relieve the symptoms. Some patients respond to medicinal treatment and careful dietetic management. Roentgenotherapy is of no value.

SCHLUTZ, Chicago.

RETICULOCYTES. LILI MICHAELIS, Ztschr. f. Kinderh. **55**:567, 1933.

The maximum number of reticulocytes in normal children, according to Michaelis, is 5 per cent. An increase in reticulocytes in a patient in whom no infection or anemia can be found is explained by the author as due to a lymphatic constitution. In such a patient, the author believes, the increase in the number of reticulocytes in the blood is due to slow maturing of the erythrocytes.

LEVINSON, Chicago.

AN UNUSUAL CASE OF HEPATOSPLENOMEGALY IN A CHILD. M. SCHOENBERG, Polska gaz. lek. **14**:559 (Sept. 4) 1935.

A 10 year old boy of Jewish origin from his eighth month had suffered from pain in the back and abdomen. Before that he was healthy. Examination showed hemangioma verrucosum and great distention of the liver, which had a smooth surface and sharp borders. The spleen was not enlarged at first. The Wassermann reaction was negative. There was no icterus. There were pronounced anemia, marked leukopenia, neutropenia and lymphocytosis. The urine was normal. There was a gradual increase in size of the liver and spleen. Examination of the marrow and of splenic tissue revealed complete atrophy of the normal morphologic elements, only large cells in the form of myeloblasts remaining, which did not take the sudan III stain. The blood cholesterol content was much increased. The general condition was good when the boy was free from fever and hemorrhages. The case is to be regarded as one of hepatomegaly, with characteristic changes in the marrow and spleen and in the fat metabolism, and may be classed with either the Niemann-Pick syndrome or the Gaucher syndrome, as it bears a resemblance to both.

VINTON, New York.

Diseases of the Nose, Throat and Ear

BACTEREMIA AND ACUTE INFECTIONS OF THE UPPER RESPIRATORY TRACT. HOWARD C. BALLENGER, Arch. Otolaryng. **20**:452 (Oct.) 1934.

The author states that most infections of the upper respiratory tract are ushered in with a cold, and he advances the idea that there may be a symbiosis of the filtrable virus causing these colds and the known pathogenic bacteria of the upper respiratory tract, the latter organisms, particularly the hemolytic streptococcus, producing bacteremia. He believes that the present methods are not adequate for the identification of these organisms in the blood stream after invasion from their local origin. Cutaneous eruptions are a manifestation of the general invasive presence of the bacteria. The frequency of appendicitis and peritonitis and, to a less extent, the involvement of the special organs, such as the heart, kidneys, brain and lungs, point to the transmission of the infection by way of the blood stream.

Warning in regard to operative procedure during or soon after infections of this kind is stressed owing to the fact that hemorrhage occurs, the reason for this being that the hemolytic streptococcus in man possesses the property of liquefying human fibrin within a short time. Perhaps this is the reason that this organism gains access to the blood stream so easily.

He concludes that bacteremia is fairly common after acute infection of the upper respiratory tract, especially when the hemolytic streptococcus is the organism in question. Unexplained fever or fever out of proportion to the clinical picture can be explained on this basis, and complications are limited only by the distribution in the blood stream.

GREENWOOD, Chicago.

PETROSITIS. MARK S. REUBEN, Arch. Pediat. **52**:689 (Oct.) 1935.

The pathology, symptomatology, diagnosis and treatment of petrositis are discussed. Five cases are presented in detail. The history of this condition is reviewed and the anatomy of the affected region described.

WADDELL JR., University, Va.

THE IMPORTANCE OF NOSE, THROAT, AND EAR EXAMINATION IN PEDIATRIC PRACTICE. ORVILLE BARBOUR, Arch. Pediat. **52**:775 (Nov.) 1935.

Not abstracted.

WADDELL JR., University, Va.

FURTHER STUDIES OF VASO-MOTOR RHINITIS IN CHILDREN. J. A. HAIMAN, Arch. Pediat. **52**:785 (Nov.) 1935.

Not abstracted.

WADDELL JR., University, Va.

WHY VINCENT'S INFECTION? P. H. BELDING and L. J. BELDING, J. Am. Dent. A. **22**:2114 (Dec.) 1935.

This brief article summarizes the contention of the authors as expressed in previous publications. It is their opinion that trench mouth and pyorrhea, both acute and chronic, are caused "by the activity of Vincent's organisms (the fuso-spirochetal complex) and should be classified and treated accordingly." They recommend the following prescription, to be used with "surgical and mechanical cleansing": solution of potassium arsenite, 40 cc.; glycerin, 60 cc., and neo-arsphenamine, 0.9 Gm.

NOYES, Chicago.

PURULENT OTITIS MEDIA IN THE NEWBORN. DANIEL J. DOLAN and MILTON J. H. GRAND, New York State J. Med. **35**:669 (July 1) 1935.

In a study of 8,000 new-born infants only one instance of purulent otitis media was found.

A new-born colored girl had a seropurulent discharge from both ears on the eighth day of life. The mother had died of streptococcic peritonitis on the seventh day post partum. The first cultures from the ear showed the same organism; later, other bacteria were also found. Bronchopneumonia developed, and the child died at 2 months of age.

AIKMAN, Rochester, N. Y.

OUR DEAFENED CHILDREN AND HOW WE ARE CARING FOR THEM. GORDON BERRY, Rhode Island M. J. **18**:182 (Dec.) 1935.

The care of deafened children, including national activities, the progress in Rhode Island and the history of the developments in this field, is briefly reviewed. A strong appeal is made for members of the medical profession to use their influence in encouraging schools and other agencies to advance the care of these handicapped children.

The program for the schools consists in testing all the children with the 4-A audiometer, having an otologist examine those whose hearing seems to be below par and referring the truly deafened for further otologic treatment. The deafened child should be seated where he can hear and see best, and classes in lip-reading should be established.

BUFFUM, Providence, R. I.

A CASE OF MASSIVE TUBERCULOSIS OF THE TONSILS. BERNARD HUDSON and F. L. WOLLASTON, Tubercle **17**:30 (Oct.) 1935.

A girl of 21 had had frequent attacks of tonsillitis, with involvement of the lymphatic glands, during a period of two years. Following two attacks of severe bronchitis a persistent cough developed with loss of weight and a slight fever.

Later the left lung became affected, and numerous tubercle bacilli were found in the sputum. Artificial pneumothorax was induced. This was followed by rapid general improvement, but the sedimentation rate of the blood remained high. Following an acute attack of tonsillitis the tonsils were enucleated. The pathologic report on these organs was: "Severe tuberculosis in the vicinity of the crypts, which has caused large caseous foci; numerous productive processes, with the development of epithelioid tubercles, scattered through the tonsils and marked with extensive giant cell formation."

From the history and pathologic observations it seems probable that the tonsils were the site of the primary lesions. In support of this theory is the rapidity with which the disease spread in the lungs, indicating a low resistance to tuberculosis, which would not likely have been the case if the infection was a reactivation of an old childhood focus in the tracheal glands. After removal of the tonsils the condition improved, and the sedimentation rate of the blood became normal.

EUGENE SMITH, Ogden, Utah.

THE VIGGO SCHMIDT TEST. P. A. SAINZ, G. PRADO and W. DOMÍNGUEZ, Med. de los niños **36**:289 (Oct.) 1935.

The Viggo Schmidt test consists of a study of the neutrophilic response in the blood count following infection and massage of the tonsils. Two counts are made early in the morning; then digital massage of each tonsil for two minutes is carried out. Leukocyte counts are made every five minutes for half an hour. In normal tonsils there is a decrease in the total number of leukocytes, especially in the lymphocytes. If the tonsils are infected the massaging produces leukocytosis and polynucleosis, with corresponding lymphopenia. This phenomenon is explained by the assumption that massage of the chronically infected tonsil liberates bacteria, toxins and products of the endolysis of polynuclear neutrophils. When these enter the circulation they have a positive chemotaxis for polynuclear neutrophils, which produces the polynucleosis.

DWYER, Kansas City, Mo.

ACUTE MASTOIDITIS AND NEPHRITIS. K. LÖWY, Monatschr. f. Ohrenh. **69**:690 (June) 1935.

Löwy analyzes 2,047 cases of acute otitis in order to determine the relationship between diseases of the ear and nephritis. He summarizes his conclusions as follows: 1. In a patient with renal disease the postoperative course of otitis is usually normal. 2. In approximately 0.7 per cent of cases of acute mastoiditis there is hemorrhagic nephritis. 3. In some of these cases otitis is the introductory infection; in some it is the primary focus, and in some it is both. 4. Otogenic nephritis occurs most frequently in children, and many of those who have the renal involvement have glandular swellings. 5. The postoperative prognosis in cases of otogenic nephritis is favorable so far as the renal disorder is concerned. 6. The existence of hemorrhagic nephritis may under certain conditions be the indication for opening of the mastoid process.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

VISIBLE EFFECT OF FARADIC CURRENT ON THE HEARING OF CHILDREN WHO ARE HARD OF HEARING. E. FRÖSCHELS, Monatschr. f. Ohrenh. **69**:735 (June) 1935.

Fröschels calls attention to a peculiar behavior observed in many so-called deaf-mutes, stating that nystagmus-like movements of the eyeballs develop if tones from the pipes of Urbantschitsch are led to the patient by means of a tube. He thinks that this symptom may be regarded as due to vestibular stimulation elicited by acoustic influences. He was able to observe this movement in about 50 per cent of the deaf-mutes. Since he has been in the habit of giving electrical treatments to patients who have severe hardness of hearing, he decided to use the faradic current also in the treatment of children who seemed to be really deaf, in that the aforementioned ocular movements were not elicitable. He gave

from fifteen to twenty faradic treatments, each one lasting for from five to ten minutes, and found that in a considerable number of the patients the test with the Urbantschitsch harmonica then elicited the ocular movements or the related swaying movements. Other patients reacted after several series of treatments with the faradic current (separated by intervals of from four to eight weeks). The author cites several cases and then states that the purpose of his report is to call attention to the fact that under the influence of faradization signs may develop that are known to be indications of hearing. He does not discuss the degree of improvement in hearing.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of Lungs, Pleura and Mediastinum

LOBAR COLLAPSE IN CHILDREN. G. L. BOYD, J. A. M. A. **105**:1832 (Dec. 7) 1935.

Basilar triangular shadows in the roentgenograms of children's chests are considered by Boyd to indicate lobar collapse. These shadows are homogeneous, opaque and in the form of a right angle triangle, with the diaphragm as the base, the mediastinum as one side and a line extending from the hilus to a point on the diaphragm as the hypotenuse. This type of lobar collapse is usually associated with bronchiectasis, and its presence in roentgenograms is suggestive of this condition. Lobar atelectasis is due to infection or trauma to the bronchial wall, with secretion and subsequent plugging of the bronchioles.

BONAR, Salt Lake City.

OBSTRUCTIVE DYSPNEA WITH ILLUSTRATIVE CASES OF THE VARIOUS TYPES. W. A. CASSIDY, Nebraska M. J. **20**:396 (Oct.) 1935.

Three cases of destructive dyspnea are reported. In the first the condition was due to bilateral paralysis of the abductor muscles of the vocal cords. Intubation was done, and nine days later, tracheotomy was performed, but the baby died within three days of bronchial pneumonia. Two cases of dyspnea from foreign bodies are reported. In the first the patient recovered promptly after the removal of an oblong piece of walnut meat. The foreign body in the other case was a quantity of minced carrot which had been aspirated two days before. The child's condition on entrance to the hospital was so alarming that an oxygen tent was used immediately rather than bronchoscopy. Particles of food were coughed up at intervals, and the child rapidly improved. When bronchoscopy was done a few days later no foreign substance was found, only an inflammatory reaction remaining.

HAMILTON, Omaha.

THE TREATMENT OF CHILDHOOD PNEUMONIA IN THE HOME. ELLSMER L. PIPER, Pennsylvania M. J. **39**:231 (Jan.) 1936.

Piper stresses that in recent years the danger of contagion in pneumonia has been generally accepted, and with the adoption of efficient prophylaxis a reduction in the morbidity may be expected. No disease has received greater attention, and in none is there a greater difference of opinion in regard to therapy. Owing to economic stress, whatever the present conception of the treatment of pneumonia may be, one thing is certain: One must be prepared to treat an ever-increasing number of patients with pneumonia in the home. The development of serum therapy, vaccine therapy and chemotherapy has resulted in many enthusiastic reports which reveal a lowered mortality; likewise, statistics are available which indicate no effect on the mortality. The value, if any, of specific and nonspecific therapy is greatest when these are instituted the first day of the disease. The final word has not yet been given on these forms of therapy. The care in the home of the patient with pneumonia demands laboratory facilities as an efficient aid in therapy. The importance of good nursing by a trained nurse cannot be overestimated. The value of well kept clinical records is as important in the home as in the hospital.

Overtreatment is especially likely in the home environment. All treatment of pneumonia must be individualized. The schedule of treatment must be planned to permit of the maximum of rest. A special effort should be made to prevent the development of the more serious symptoms, which may be accomplished by the forcing of fluids, efficient elimination, hydrotherapy, alkalinization with milk and a proper diet. Expectorants are mentioned, only to be condemned. If sufficient water cannot be given per orem, it must be given by enteroclysis or hypodermoclysis, with the addition of 75 per cent solution of dextrose in physiologic solution of sodium chloride. The principal indications for oxygen therapy are rapid, shallow respirations, anoxemia and beginning cyanosis. The intramuscular administration of whole blood, in amounts of from 20 to 40 cc., seems to be of value in delayed resolution. A complete blood count is indicated during convalescence to determine the degree of secondary anemia or other abnormal blood findings, and proper treatment should be instituted.

LOGUE, Williamsport, Pa.

CONGENITAL CYSTIC LUNG. ALISTAIR ARGYLL ROBERTSON, Brit. M. J. **2**:837 (Nov. 2) 1935.

"The term 'congenital cystic lung' is used for cases in which occlusion cysts appear in the lungs—that is, cysts which have no communication with the bronchi—and for cases of congenital bronchiectasis in which the dilated bronchi appear as cysts."

The report of a case is given with a discussion of the history, clinical notes and observations at autopsy. The author concludes with the following pathologic report:

The following is the report on the microscopical examination of the left lung: *Upper lobe.*—The 'cysts' are obviously dilated bronchi, and for the most part lined by a layered bronchial mucosa. In places the mucosa is missing and the 'cysts' are then lined by inflammatory granulation tissue, in which are numerous large cells having a markedly vacuolated cytoplasm and which appear to be macrophages. Pus is present in some of the cysts, together with remnants of injection material. Alveoli are present, but tend to be collapsed; some of them are lined by cubical epithelium suggesting that they were not functioning. *Lower lobe.*—Acute bronchopneumonia with early fibrosis in parts. Bronchial and cervical lymph glands; oedema and hyperaemia; there are none of the giant cells described by Collins."

ROYSTER, University, Va.

SOME RECOLLECTIONS ON ASTHMA, WITH A FEW SUGGESTIONS AS TO ITS TREATMENT IN CHILDHOOD. W. D. ALLAN, Glasgow M. J. **6**:225 (Nov.) 1935.

In considering the etiology of asthma Allan discusses heredity, the nose, trauma and the endocrine glands. With regard to the nose, there is an area on the upper posterior portion where electrical stimulation causes bronchospasm. Traumatic factors may also play a part. Asthma may develop after pneumonia, whooping cough, abortions, the menopause and the male climacteric.

The endocrine factor is linked with the activity of the autonomic nervous system. Late research has shown that thyroid, pituitary and ovarian secretions play a rôle in bronchospasm. The author noted two types of patients: the thin type, with a dry skin, and the obese type, with a nervous disposition.

Treatment consists in clearing up foci of infection, feeding a diet low in carbohydrate, forbidding foods that are known to upset the child and giving six injections of bronchial asthma vaccine. This is augmented with injections of the sex hormone, male or female, given weekly or biweekly for three months, and from one-third to one-half dose for adults of a mixed tablet consisting of extract of anterior pituitary, adrenal, thyroid and ovarian glands, given orally.

Allan has used this routine in thirty children, with success; he feels that the sex gland material is of definite value.

SNELLING, Toronto, Canada.

THE VALUE OF BREATHING EXERCISES IN ASTHMA. MARJORIE GILLESPIE, Lancet **2**:705 (Sept. 28) 1935.

During an attack of asthma, in which the bronchioles are narrowed by spasm and congestion, there is a valvular action whereby air drawn in by strong inspiration can enter the alveoli but cannot escape.

The aims of the breathing exercises are: (1) to empty the lungs by increasing the expiratory phase; (2) to reeducate the automatic diphragmatic movements and to diminish the thoracic type of breathing; (3) to relax spasmodically contracted muscles; (4) to mobilize the ribs and the wall of the chest and to correct kyphosis.

In seventy-five patients with asthma who were treated for one year with expiratory breathing exercises, good clinical results were obtained in fifty-two, improvement in twelve and no improvement in eleven. Improvement seemed to depend on the patient's acquiring mobility of the chest, natural diaphragmatic breathing and control of the diaphragm. There is also a considerable psychologic factor. In addition, of course, specific treatment should not be neglected.

LANGMANN, New York.

TREATMENT OF METEORISM AND PARALYTIC ILEUS OCCURRING DURING BRONCHOPNEUMONIA IN CHILDREN. SCHNEEGAN and B. TASSOVATZ, J. de méd. de Paris **55**:918 (Oct. 17) 1935.

This is a brief review of various methods of combating meteorism. The application of heat to the abdomen, the use of the rectal tube, high enemas, the administration of extract of posterior pituitary and physostigmine and lumbar anesthesia are considered.

LESLIE, Evanston, Ill.

PYOPNEUMOTHORAX IN THE INFANT. MARIA ISABEL CRUZ, Arch. de pediat. d. Uruguay **6**:351 (Aug.) 1935.

The author describes four cases of pyopneumothorax occurring in infants between the ages of 9 and 22 months. One patient recovered. In this case the condition was an encysted form, and treatment was by simple thoracentesis and evacuation of the pus. All the other cases terminated fatally.

SCHLUTZ, Chicago.

SPONTANEOUS PNEUMOTHORAX IN EARLY INFANCY. CARLOS GIANELLI and JULIO R. MARCOS, Arch. de pediat. d. Uruguay **6**:421 (Oct.) 1935.

Gianelli and Marcos report three cases of the fairly rare condition spontaneous pneumothorax, two occurring in infants over a year old and one in an infant 1 year old. One patient had a positive tuberculin reaction, and two had a negative reaction. In all three cases the pneumothorax occurred on the right side. In one case the condition was of the valvular type. Dyspnea was the most distressing symptom. Tuberculosis and pulmonary abscess are the most likely etiologic factors. The prognosis is generally grave, and surgical procedure is required to evacuate the gas or pus. In two cases the condition ended fatally; one patient recovered.

SCHLUTZ, Chicago.

ALLERGIC PULMONARY INFILTRATIONS IN CHILDREN. HANS-ULRICH KÖTTGEN, Ztschr. f. Kinderh. **55**:483, 1933.

Köttgen comes to the conclusion that there is a definite relationship between lobar pneumonia and tuberculosis of the lung, not only with respect to localization but also as to origin. In both diseases there is an original interpulmonary focus around which develops an extensive infiltration. Both diseases have as their origin an allergic process of the whole body which localizes in a single lobe of the lung because of specific local conditions.

LEVINSON, Chicago.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

CONGENITAL OBSTRUCTION OF THE BILE DUCTS. WILLIAM E. LADD, Ann. Surg. **102**:742 (Oct.) 1935.

According to observers, the bile ducts in their process of development pass through a solid stage. If normal development continues, this solid cord becomes vacuolated; the vacuoles coalesce, and the lumen becomes reestablished. An arrest in development during the solid stage more adequately explains the malformations found than any of the other theories advanced.

While it is difficult to make a diagnosis in the first few weeks of life, this becomes simpler as the infant grows older. Jaundice may be present a few days after birth but does not become marked until the infant is 2 or 3 weeks old. The stools are acholic, and the urine is dark and gives a positive reaction for bile. The bleeding time and the clotting time are slightly prolonged. Such diseases as icterus neonatorum, erythroblastosis, the jaundice of hemolytic sepsis and congenital syphilis must be considered in the differential diagnosis. If one delays making a final diagnosis of congenital biliary obstruction until the infant is from 4 to 6 weeks old the chance of error is not great.

When the diagnosis has been made, the next step is exploratory operation, as 100 per cent mortality may be expected unless the obstruction is relieved. It is better usually not to operate before the end of the first month, as nothing is lost by this delay and assurance of a correct diagnosis is gained. It is not wise to wait beyond the second month, as nothing can be gained by further delay in arriving at a correct diagnosis and delay may result in death in those infants who have a low resistance to infections.

The study of forty-five cases is reported.

BANTIN, Omaha.

OUTBREAK OF FOOD POISONING FOLLOWING A CHURCH SUPPER. Health News **12**:173 (Nov. 4) 1935.

Following a church supper in a town in western New York at least eighty of the three hundred persons who attended had nausea, abdominal cramps, chills and vomiting. A through study showed that chicken that had been served was responsible. Staphylococci, together with a gram-negative bacillus with characteristics of Bacillus proteus, were isolated from the chicken.

AIKMAN, Rochester, N. Y.

ANOREXIA IN CHILDREN. H. B. HAMILTON, Nebraska M. J. **20**:385 (Oct.) 1935.

Anorexia is sometimes only apparent. The child may be of good weight and condition but is taking a concentrated diet, and the mother thinks that he does not eat enough. Anorexia may be caused by illness, either acute or chronic, for instance, some infection or anemia. The third and largest group is that of the children in whom no organic basis for the anorexia can be found, and the condition is due to the fact that nervous mothers are attempting to fit the child to food and a regimen rather than fitting the food and regimen to the child. Strenuous efforts to fit the child to standards are used to an unreasonable degree. Common sense should prevail in the management of these children.

AUTHOR'S SUMMARY.

PYLORIC STRICTURE FOLLOWING THE INGESTION OF MURIATIC ACID. JAY M. ARENA, South. M. J. **29**:331 (March) 1936.

The ingestion of acid even in small quantities or low concentration may be followed by the formation of scar tissue somewhere in the stomach without involvement of the esophagus. The acids seem to have only a scorching effect

on the esophageal mucosa, and their effect is concentrated on the pylorus. Operation for pyloric stricture seems to be the treatment of choice. Arena reports success by this treatment in a boy aged 2 years who had swallowed muriatic acid.

SCHLUTZ, Chicago.

INTUSSUSCEPTION. P. L. HIPSLEY, Brit. M. J. **2**:717 (Oct. 19) 1935.

A study of 486 cases of intussusception treated by ten surgeons is reported. Three of the surgeons made a practice of using a preliminary injection of saline solution by rectum before operation. The combined mortality rate in their cases was 9.8 per cent. The other 7 surgeons operated on all patients without a preliminary injection. The combined mortality rate in their series was 14 per cent.

"The results in the cases treated by the three surgeons who used preliminary saline rectal injections are as follows:

"*Surgeon A* treated 42 cases, and reduced 45.2 per cent. by injection: reduced without operation, 10; found reduced at operation, 9. Unreduced by injection, 23.

"*Surgeon B* treated 46 cases, and reduced 43.4 per cent. by injection: reduced without operation, 13; found reduced at operation, 7. Unreduced by injection, 26.

"*Surgeon C* treated 83 cases, and reduced 57.8 per cent. by injection: reduced without operation, 35; found reduced at operation, 13. Unreduced by injection, 35."

Hipsley outlines his personal series of cases, 54 in number, as follows: reduced without operation, 20; found reduced at operation, 14; unreduced at operation, 20. Reduction by injection was obtained in 62.9 per cent of these cases. Then follows the discussion of recurrent, irreducible and fatal intussusception, a consideration of the varieties, etiology, symptoms and diagnosis of this condition and, finally, a description of the technic of the use of hydrostatic pressure, which is as follows:

The rectal injection is administered only under a general anesthetic. Pressure is obtained by a column of water from a height of 3 feet and 6 inches (106.7 cm.). A catheter is inserted into the rectum for about 2 or 3 inches (5.08 or 7.6 cm.), and the buttocks are pinched together around the catheter so that no fluid escapes during the injection. No lubricant is to be used on the catheter. Saline solution is allowed to run into the bowels for three or four minutes after disconnection of the catheter. The saline solution is returned into a bedpan. A second and a third injection are given, the whole process taking about ten minutes. The first return usually contains blood; the second is clearer and may contain a few specks of fecal material, and the third contains more feces, with, perhaps, flatus, indicating probable reduction.

The indication of reduction depends on the fact that some of the saline solution passes through the ileocecal sphincter and distends the small intestine, and as a result there is decided distention of the abdomen. Measurement of the abdomen before and after the treatment shows a difference of from 1½ to 2 inches (3.8 to 5.08 cm.). In cases in which the tumor is present before the administration of saline solution is begun and reduction occurs, the tumor has disappeared when the enema is discontinued. Apparently the author feels no uncertainty about this procedure and believes that in his hands and those of his colleagues the treatment is successful.

ROYSTER, University, Va.

ANOREXIA IN THE INFANT. P. LEREBOULLET, Arch. de méd. d. enf. **38**:645 (Nov.) 1935.

Two groups of infants found in all clinics are compared. In the first, the babies are vigorous; they are easily fed, regardless of the formula, and respond readily to a change of regimen and environment, adapting themselves to treatment. In the other group the patients have lost their appetite and obstinately refuse all forms of nourishment; in consequence of this disability, combined with such other disorders as may exist, they reach a condition of progressive hypotrophy which readily challenges one's resources.

The latter type not only refuse the feedings but soon show nervous phenomena marked by great agitation and restless sleep and later on suffer from disturbances of digestion, such as vomiting and diarrhea. Finally the infant becomes cachectic to a degree which disquiets all concerned with its management. Only the return of appetite and of normal assimilation can prevent a catastrophe.

The sources of this anorexia are numerous, and they must be accurately determined in each instance. An intensive psychologic investigation is imperative, rather than the hit-and-miss administration of drugs. Lereboullet reports a series of cases illustrating this curious but frequent syndrome. In addition to those instances of purely psychic origin, he cites others in which the rôle of general debility, acute or chronic infections, overfeeding or underfeeding, aerophagia, avitaminosis, local irritations or the eruption of teeth play a part. In the majority of cases, however, the psychic element constitutes to a considerable degree an important part in the genesis of anorexia.

AMESSE, Denver.

THE DI-METHYLCARBAMIC ESTER OF 3-OXYPHENYL-TRI-METHYLAMMONIUM METHYLSULFATE IN THE TREATMENT OF INTESTINAL OBSTRUCTION OF INFANTS DUE TO DRUGS. C. MASSIAS, J. de méd. de Paris **55**:214 (March 7) 1935.

It is not rare, according to the author, to find among Annamite infants obstruction of the intestine due to paralysis of the motor nerves from absorption of certain Chinese drugs. Good results are obtained from the subcutaneous injection of 0.25 methylammonium methyl sulfate. This is given following a small retention enema of glycerin or of a 10 per cent solution of sodium chloride. Infants with abdomens that were enormously distended for two days passed stools within two hours following the injection of this drug.

LESLIE, Evanston, Ill.

CYCLIC VOMITING IN CHILDHOOD AND ERRORS IN DIAGNOSIS. P. NAU, J. de méd. de Paris **55**:823 (Sept. 19) 1935.

The history of previous attacks of cyclic vomiting does not warrant the assumption that the recurrence of similar symptoms is necessarily of a similar benign nature. Nau recalls one of his cases in which acute poliomyelitis of the bulbar type was mistaken for a simple attack of cyclic vomiting. He also calls attention to the group of cases of hepatonephritis reported by Turquety which, though characterized by symptoms similar to those of cyclic vomiting, may be differentiated by hematemesis, massive albuminuria and hypothermia. Furthermore, any acute infection in children with the constitutional tendency to cyclic vomiting may start with all the appearances of a simple attack. For this reason these children require special care and frequent examination.

LESLIE, Evanston, Ill.

ANATOMIC STUDY OF HYPERTROPHIC PYLORIC STENOSIS IN THE INFANT. AUGUSTIN CASTELLANOS, ALVARO SILVA and JUSTO PAUSA, Bol. Soc. cubana de pediat. **7**:255 (Aug.-Sept.) 1935.

Four types of hypertrophic pyloric stenosis can be distinguished. In the circular, or classic, type there is a tumor which has little vascularization and greatly increased circular fibers.

In the Landerer-Mayer type there is no tumor but rather diminution or athrepsia of the pylorus.

In the longitudinal type of Finkelstein the tumor is vascular, especially on the convex side, and the longitudinal fibers are increased.

A fourth type, described by the author, presents the picture of a tumor the size and shape of a large almond and containing an increase of radial and oblique fibers.

SCHULTZ, Chicago.

CELIAC DISEASE. MARTÍNEZ VARGAS, Med. de los niños **36**:326 (Nov.) 1935.

The history of celiac disease is reviewed briefly, and two typical cases are reported. Among the various means of treatment mentioned are the following: opiates and atropine, to retard the hypermotility of the intestinal tract; magnesium, sodium and bile salts, to facilitate the emulsion of fats; insulin, because of the possible pancreatic deficiency and also to promote absorption of water from the intestine; other gland extracts, particularly epinephrine; tri-calcium phosphate and iron, to combat demineralization; ultraviolet rays; antisyphilitic therapy, when syphilis accompanies the celiac disease; blood transfusions and the injection of dextrose subcutaneously and intraperitoneally, and, finally, the Trendelenburg position at times.

DWYER, Kansas City, Mo.

FOREIGN BODY INCARCERATED IN THE ESOPHAGUS. G. GAEHTGENS, Centralbl. f. allg. Path. u. path. Anat. **63**:5, 1935.

A coin (10 *Pfennigstück*) was found in the esophagus of a child 1½ years old who died of myocarditis following pharyngeal diphtheria. There was no history of the coin's being swallowed or of symptoms referable to such an act, which must have occurred a considerable time before the terminal illness. The coin was firmly embedded in the esophageal mucosa, on the anterior part between the cricoid cartilage and the bifurcation. Although it was embedded so deeply that it was removed with difficulty, there was no erosion of the tracheal cartilage.

RUKSTINAT, Chicago. [ARCH. PATH.]

DUODENAL ULCER IN CHILDREN. WALTER HIRSCH, Monatschr. f. Kinderh. **63**:429, 1935.

A review of the literature on duodenal ulcer and the reports of cases of this condition in two boys aged 14 and 15 years, with the roentgen findings, are given. For a long time the symptoms were considered to be those of gastric neurosis. The symptoms in the child are much the same as those in the adult, the essential points being the history of pain and the roentgen findings. Chronic appendicitis must be ruled out. Among dietetic measures the use of vitamin C is particularly recommended. Operative procedure does not give as favorable a result in the child as in the adult.

GERSTLEY, Chicago.

THE ANTIGENS AND ANTIBODIES OF TAPEWORMS. O. SIEVERS, Ztschr. f. Immunitätsforsch. u. exper. Therap. **84**:208, 1935.

Rabbits inoculated with mixtures of alcoholic extracts of Diphyllobothrium latum and of Taenia saginata with hog serum or with watery suspensions of tapeworm tissue produced immune serums that reacted specifically by means of the complement fixation test with alcoholic extracts of various tapeworms. Under proper quantitative conditions the immune serums reacted in a species-specific manner with the homologous antigens. The species specificity of the T. saginata antiserums was more pronounced in the precipitation reaction, while in the case of the D. latum, the complement fixation reaction was more suitable. Attempts were made to demonstrate antibodies or antigens in the blood serums of persons suffering from infestation with D. latum. The results were not sufficiently specific to be of practical value.

DAVIDSOHN, Chicago. [ARCH. PATH.]

CUTANEOUS ALLERGY AND THE COMPLEMENT FIXATION TEST IN THE DIAGNOSIS OF INFESTATIONS WITH TREMATODES. O. WAGNER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **84**:225, 1935.

The reactions to intracutaneous injections of extracts of the liver fluke (Fasciola hepatica) were not specific. They occurred in 73 per cent of infected sheep, but they also occurred in sheep free from the parasite. Positive reactions were observed also in sheep infested with other species of trematodes. The complement

fixation test gave similar results, but a combined use of both procedures increased the incidence of positive results in the infected animals to 90 per cent. Both tests lack practical significance in view of the fact that examination of the feces makes it possible to establish the presence of the parasites quite easily. Wagner calls attention to a possible application of both tests in those cases of trematode infestation in man in which a homologous antigen is not easily obtainable.

DAVIDSOHN, Chicago. [ARCH. PATH.]

ROENTGENOSCOPY OF THE COLON IN INFANTS. K. GEFFERTH, Orvosi hetil. **79**: 349 (March 30) 1935.

The rugae of the mucous membrane of the colon of infants are not as decided as later. The whole picture is simpler. The definite haustration is missing, and one can see only its washed-out sketch. The inclination to contraction appears only in the wavy run of the folds. The colon changes its shape quickly; it can relax in a short time and fill with gas. An elongated and dilated sigmoid is often found in infants.

GÖTTCHE, Budapest, Hungary.

Nervous Diseases

OTOGENOUS ABSCESS OF THE PARIETAL LOBE. CYRIL B. COURVILLE and J. M NIELSEN, Arch. Surg. **30**:930 (June) 1935.

Six cases are reported in which the parietal lobe was the location for an abscess secondary to otitis media. Because of the distance between the middle ear and the parietal lobe Courville and Nielsen suggest a vascular route for the transmission of the infection. Infection enters the venous radicle draining the middle ear and extends to the parietal region. Otogenous abscess of the parietal lobe is frequently associated with one or more cerebral abscesses, which results in a complex clinical picture. The characteristic symptoms of abscess of the parietal lobe thus far determined are jacksonian seizures affecting the contralateral members, often associated with deviation of the head toward the convulsing members, followed by monoplegia brachiofacialis, deviation away from the paralyzed side, sensory manifestations and at times aphasia.

KAISER, Rochester, N. Y.

ETIOLOGICAL CONSIDERATIONS OF HEADACHE. FREDERICK TILNEY, Bull. New York Acad. Med. **11**:500 (Aug.) 1935.

This paper is part of a symposium on headache. The theories of pain are discussed in general and the unitary neural theory in particular, with reference to headache. (1) Causes affecting the head directly. Intracerebral lesions, tumors of the brain, abscess and cysts. Headache due to these causes tends to become localized, and sometimes there are areas of local tenderness corresponding to the location overlying the lesion. Headache due to tumor of the brain is not continuous; there is a certain degree of periodicity, and there may be remission of considerable length, with subsequent return of the pain with great intensification. The author warns, however, that headache due to tumor of the brain is subject to so many and such confusing variations that no hard-and-fast rule can be laid down for its identification. The pain may be entirely absent in the case of a large growth, and it may be intense in the presence of a very small tumor. Abscess of the brain is somewhat more consistent in its manifestation of symptomatic headache, although in this condition too the degrees of congestion, extravasation and edema may give rise to variable symptoms. Cyst of the brain produces headache by spinal fluid block. The inflammatory changes in the brain (encephalitis) or its coverings produce diffuse or localized pain in the head by virtue of changes in cerebral tension. (2) Causes arising in or primarily affecting parts of the body other than the head, such as bacterial toxins (febrile con-

ditions), chemical poisons (gastro-intestinal tract and kidneys) or endocrine imbalance. (3) Causes incident to lumbar puncture or injection of air. (4) Psychogenic causes. The last three factors cannot be explained on the theory of the neural mechanism.

JAHR, Omaha.

DELAYED MENINGEAL SYNDROME OF INSOLATION. J. CATHALA, A. BOSQUET and M. KIRYCZANSKI, Arch. de méd. d. enf. **38**:530 (Sept.) 1935.

The usual reaction of the meninges to sunstroke is expressed in such easily recognized manifestations as vertigo, great weakness, headache, congestion of exposed surfaces, vomiting, delirium and convulsions. Dopter has demonstrated that there are also changes in the spinal fluid, directly proportionate to the degree of injury; in the benign form there may be only a slight increase in pressure, but in the graver types of insolation it is common to find an increase both of tension and of the cellular elements and, in addition, changes in the albumin content.

Without an accurate history a diagnosis of acute cerebrospinal meningitis would promptly be given in these cases. The difficulty of classification is particularly noted, however, in the cases in which the condition has apparently progressed to complete recovery and symptoms of meningeal irritation subsequently develop. The authors report such an instance in a boy of 15 years, admitted to the hospital with a tentative diagnosis of typhoid. He had sustained a severe attack of sunstroke six days prior to his admission. Enteric fever and acute arthritis were readily excluded, but on the seventh day rigidity of the neck with Kernig's sign was noted, and lumbar puncture released a grayish, opalescent fluid, containing a large number (the exact number is not stated) of polymorphonuclear cells. Smears and cultures showed nothing abnormal. The following day, the lad sat up in bed and read a newspaper, but a second puncture showed 300 cells per cubic millimeter. He was discharged from the hospital the following week, and on reexamination six months later, he was in excellent health.

AMESSE, Denver.

PSEUDOMYOPATHIC POLYNEURITIS. ROBERT DEBRÉ, JULIEN MARIE and MESSIMY, Bull. Soc. de pédiat. de Paris **32**:322 (June) 1934.

A boy, 5 years old, began to have difficulty in walking. This became progressively worse, and the muscles about the pelvic girdle gradually became involved so that he could not pick himself up from the dorsal decubitus position without turning on his abdomen and pushing his hands against his knees and thighs. This condition resembles that found in myopathic disease. All the tendon reflexes were abolished. The greatest muscular weakness was present about seven weeks after the onset. He recovered completely after a few months. The comparatively rapid onset of the symptoms, and the complete absence of reflexes, followed by their subsequent reappearance with the recovery of muscular power, were in favor of a diagnosis of polyneuritis. The etiology was probably toxic.

BENJAMIN, Montreal, Canada.

ACUTE PRIMARY MENINGITIS DUE TO THE BACILLUS OF PFEIFFER: CURE. M. NOBÉCOURT and P. DUCAS, Bull. Soc. de pédiat. de Paris **32**:596 (Dec.) 1934.

A girl, 5 years old, was admitted to the hospital twenty days after the onset of illness. There was stiffness of the neck, and lumbar puncture yielded a somewhat turbid fluid containing many cells, most of which were polymorphonuclear leukocytes. Stained smears of the spinal fluid showed pleomorphic coccobacilli, characteristic of the bacillus of Pfeiffer. The child made a complete recovery, which is noteworthy in view of the high mortality of this disease. Repeated spinal drainage was performed, and at first intrathecal injection of polyvalent

antimeningococcus serum was given. Cultures of material from the nose and throat revealed no meningococci or Bacillus influenzae. Cultures of the spinal fluid failed to produce the organism, which was repeatedly demonstrated in smears in large numbers. It may be that during the long period from the onset of the illness to the first lumbar puncture the organism became attenuated, or possibly the virulence was slight. This is offered as a possible explanation of the inability to grow the organism in culture and of the fact that the child recovered.

BENJAMIN, Montreal, Canada.

A TEMPORARY SPINAL FISTULA FOR CONTINUOUS DRAINAGE OF THE SPINAL CANAL. S. STEFANINI, Riv. di clin. pediat. **33**:1 (Jan.) 1935.

Continuous drainage of the spinal canal is frequently desirable in cases of hydrocephalus and meningitis. For this purpose the author has devised a cannula which may be kept in place for several days. The apparatus consists of a lumbar puncture needle specially made for the purpose. Attached to the needle is a wide disk, serving as a guard. In the disk are small holes so that the cannula may be held in place by threads attached to a belt. The outlet of the cannula is constructed to allow the attachment of a rubber tube, connected with a manometer and stopcock, which regulates the rate of flow of the spinal fluid. The child lies on his side on a Bradford frame, and the needle is inserted in a lumbar interspace.

The cannula did not seem to cause the child any definite discomfort, even when it was used for a long period; in one case it was in place seventeen days.

The cannula was employed clinically in cases of acute and chronic hydrocephalus associated with tuberculous meningitis and in cases of purulent meningitis. In two cases of acute hydrocephalus benefit resulted from use of the fistula, and the balance between the formation and the absorption of spinal fluid became adjusted while the cannula was in place, while in other cases of hydrocephalus no definite benefits were obtained. In a case of tuberculous meningitis the child did not improve. In purulent meningitis good results were obtained only in cases of meningococcic meningitis; in these instances the continued drainage proved of great benefit. In one case 5,380 cc. of spinal fluid was withdrawn during seventeen days, an average of 316 cc. each day.

HIGGINS, Boston.

ACUTE MOTOR CEREBROSPINAL POLYNEURITIS OF TOXIC NATURE, WITH AN APOPLECTIFORM ONSET, IN A GIRL OF TWO YEARS (ATEBRINE POISONING). S. MOSCHINI, Riv. di clin. pediat. **33**:823 (July) 1935.

A girl of 2 years had an attack of malaria early in June and was treated by quinine given by mouth. On July 8 a recurrence of the malaria occurred, and the child received atebrine in doses of 0.15 Gm. daily for six days. The child recovered from the febrile attack and, although she was yellow for a while, showed no untoward symptoms. On August 21 another attack of fever was manifest, and again atebrine was given in the same doses as previously. After the third dose the child vomited the medicine. That night she became very thirsty and drank considerable water. The following morning she showed marked tremors of the legs and weakness. Extensive paralysis developed, which extended to practically all the muscles in the body. The child became very yellow, and the maximum degree of paralysis was reached on August 28.

Considerable difficulty was experienced in caring for the child, especially in the giving of nourishment. She showed distinct weakness of the muscles of respiration when excited. Recovery from the paralysis was gradual, and it was not until November 16 that she could be discharged home from the hospital. On the the following May 29 she still showed some hypotonia and generalized muscular atrophy. She had, however, recovered power in practically all her muscles.

Moschini believes that the child had polyneuritis in which the paralysis simulated Landry's syndrome and was apparently due to the toxic effect of atebrine. The action of this drug is compared with that obtained experimentally with curare.

HIGGINS, Boston.

EPILEPSY FOLLOWING SEROUS MENINGITIS. M. SCHACHTER, Med. de los niños **36**:193 (July) 1935.

A case of epilepsy in a child, aged 5 years, following an attack of serous meningitis, is reported. Meningitis occurred when the child was 18 months old. Shortly thereafter hydrocephalus developed, which was relieved by lumbar and ventricular punctures. The child appeared to be recovering when chronic convulsive attacks occurred at the age of 30 months. These have continued as generalized convulsions lasting twenty seconds and have not yielded to treatment with barbiturates or diet therapy.

DWYER, Kansas City, Mo.

SYDENHAM'S CHOREA. JULIO DANERI, Rev. chilena de pediat. **6**:107 (March) 1935.

As symptomatic treatment in cases of Sydenham's chorea, the author advises the use of opium derivatives, chloral hydrate, scopolamine hydrobromide and bromides. He regards the intraspinal use of magnesium sulfate as dangerous. Phenobarbital combined with antipyrine gives good results.

The etiologic treatment presumes the establishment of a specific causative factor. If rheumatic symptoms are pronounced salicylates are indicated. If there is evidence of syphilis this must be adequately treated. Arsenicals always seem to be effective, especially in the chronic forms. The use of solution of potassium arsenite, sodium cacodylate and neoarsphenamine is of value. Removal of possible focal infections, such as diseased teeth, tonsils and sinuses, is indicated. In refractory conditions, the author recommends hyperthermia produced particularly by the use of vaccine or other foreign protein.

SCHLUTZ, Chicago.

ENCEPHALITIS IN CHILDHOOD. J. ZAPPERT, Wien. klin. Wchnschr. **48**:824 (June 14) 1935.

Zappert states that recent histologic investigations have resulted in a distinction between genuine encephalitis with cellular infiltration and pseudo-encephalitis. There are primary epidemic encephalitis, encephalitis associated with Heine-Medin disease and encephalitis following vaccination. The clinical picture is not restricted to the brain but may include the meninges and the spinal cord. The symptomatology is complex; there may be the toxic-convulsive, somnolent-paretic and hemiplegic forms of the disease and a form resembling Landry's disease; there may be acute cerebral tremor, acute ataxia and myelitic conditions, or there may be less severe abortive forms (encephalitis ambulatoria). Especially important are the following forms: (1) Epidemic lethargic encephalitis (Economo's disease), which appeared in epidemic form in many parts of Europe from 1916 to 1922, expressed itself mainly in lethargico-ophthalmoplegic and irritative hyperkinetic syndromes and may lead to peculiar resultant conditions, such as parkinsonism, insomnia, changes in personality, convulsive movements and adiposity. It rarely appears now in epidemic form. (2) Encephalitis following vaccination, which has been observed since 1924 in England, Netherlands and other countries. The number of cases has been large, although it is small in proportion to the number of vaccinations. In some regions the mortality is high, although in the cases in which cure has resulted there are no bad after-effects. The cause of the disease is unknown. The assumption of a specific vaccine disease (Eckstein) and that of parallergic activation of a latent encephalitic virus (Keller) are both unsatisfactory. Priesel, Lucksch and Bogaert considered the possibility of an allergic-toxic reaction of the central nervous system analogous to an exanthematous reaction of the skin. (3) Para-infectious forms of encephalitis occurring after the less severe infectious diseases, such as measles, chickenpox, mumps and German measles. Except for encephalitis following measles these forms are not dangerous. From a pathologico-anatomic point of view, the postvaccinal and para-infectious types of encephalitis show similarity, although both are differ-

ent from epidemic lethargic encephalitis. (4) Spontaneously appearing encephalomyelitis disseminata has been frequently observed in recent years. Symptomatologically, it presents features already noted in other forms of encephalitis.

ABT, Chicago.

DISEASES OF THE GROUP OF PSEUDOSCLEROSIS (WILSON) IN YOUNG CHILDREN. W. J. C. VERHAART, Ztschr. f. d. ges. Neurol. u. Psychiat. **150**:493 (July) 1934.

Verhaart reports three cases of pseudosclerosis in Chinese children—a boy aged 4 years, a girl aged 8 months and a girl aged 7 months. All showed a tendency to extension of the extremities and of the trunk, with pathologic reflexes in both feet. There were accompanying symptoms of involvement of the brain, dulness, strabismus, high fever and vomiting. Histopathologically, in all three cases there were the end-results of a severe phagocytosis in the brain and complete degeneration of the tissues into fat. There were a large number of granular cells and little evidence of activity on the part of the fixed glia cells in the removal of the fat. The etiology is unknown; in the absence of inflammatory reactions a toxic agent is postulated. MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

MENINGISM OF HELMINTHIC ORIGIN. F. D. ZAU, Chinese M. J. **49**:689 (July) 1935.

The author has made a survey of forty-three cases in which symptoms of meningeal involvement were apparently due to infestation with helminths. He prefers the term meningism of helminthic origin, to that of meningitis due to infection with Ascaris. In association with two other physicians he studied the possible relation of symptoms of meningeal involvement to the presence of various intestinal and blood parasites. The symptoms disappeared after the use of vermifuges for the known infestation with Ankylostoma or Ascaris. Lumbar puncture was performed in all cases. Two cases of meningism caused by infection with relapsing fever were also included. NEFF, Kansas City, Mo.

Psychology and Psychiatry

THE PSYCHOANALYTIC PSYCHOLOGY OF THE YOUNG CHILD. SIEGFRIED BERNFELD, Psychoanalyt. Quart. **4**:3 (Jan.) 1935.

Bernfeld outlines the psychoanalytic attitude toward children. Three main points characterize this attitude:

1. Psychoanalysis knows no ethical value. It is a scientific method of observation, during which behavior is regarded impartially as neither good nor bad. He emphasizes that this does not mean that the individual psychoanalyst is lacking in standards, nor does he sanction everything in life.

2. Psychoanalysis is the genetic view of all phenomena consistently developed. It attempts to trace the development of behavior and find in all behavior a common origin. Less value is placed on divergencies of behavior sometimes present in children than on the common origin.

3. Psychoanalysis observes the development of children with pessimism, but it is pessimism based on scientific observation. "It is extremely difficult to treat and influence men and women, and it is no easier to treat and influence small, even very small children."

The author emphasizes sex impulses as one of the important influences in behavior. The oedipus situation is explained. BEVERLY, Chicago.

PSYCHOANALYSIS AND THE TRAINING OF THE YOUNG CHILD. ANNA FREUD, Psychoanalyt. Quart. **4**:15 (Jan.) 1935.

The author states that in training, instinctive impulses and satisfactions should not be suppressed or given complete satisfaction, as both methods lead to fixation

at a low level of development. Should the educator use fear for purposes of prohibition? The answer is found in the oedipus situation. The child takes to himself the object—the parent or person in charge of his training. He takes over from them commands and prohibitions. His first fear tending to produce obedience is that of being left alone and of losing love if he disobeys. This gives the teacher a great deal of power over the child.

Teachers of young children are more important than those of older children, yet they receive less consideration from society. The reason may be that they are allowed nothing to say about education except the pedagogic method. They are given the raw material, and society decides the end-results. The demands of society vary, and teachers attempt to obtain the desired result. They fail and turn to psychology for help. Only through psychology and the understanding of the capacity and the nature of minds, of development and of individual children will it be possible to point out the impossibility of this attempt to meet the requirements of adult society for education.

BEVERLY, Chicago.

PROFOUND DISTURBANCES IN THE NUTRITIONAL AND EXCRETORY HABITS OF A FOUR AND ONE-HALF YEAR OLD BOY: THEIR ANALYTIC TREATMENT IN A SCHOOL SETTING. ANNI PÖRTL, Psychoanalyt. Quart. **4**:25 (Jan.) 1935.

A 4½ year old boy entered kindergarten, who walked with his body at right angles to his legs and in a rigid position, such as one sees in the adult suffering from catatonia. He wet and soiled himself and refused to talk or to leave his mother. He was illegitimate; the father had deserted the mother, and the parents were very poor. He slept with his mother. In kindergarten, as he became attached to the teacher, he began to talk, became continent and did well until he had an attack of tonsillitis, when all the old symptoms returned. He had to be forced to eat. It was later brought out that he would not eat because of the fear that he would have to urinate or defecate. In games he played "toilet." It was later found that he would not touch the penis. The history was finally obtained that the incontinence developed after a convulsion two years before. The mother was given instructions on caring for the penis, which was repulsive to her. This disgust and her punishment for masturbation and her scaring him by telling him that he would lose his penis and that it was nasty were the cause of his fear to touch himself. His behavior was explained to him, and after a great deal of effort he was willing to touch himself. The boy's progress was interrupted many times by illness, after which he always became worse; but each regression was less marked than the preceding. He often became violent after his behavior was explained to him. When the reason for this was explained, the outbreaks slowly subsided, but to this point his games and play centered about his genitals. He finally, however, showed social inclinations. He became interested in what the other children were doing. He slowly began to talk, at first with much embarrassment. Later, he expressed the wish to be a baby again (to grow up again without the unpleasant experiences). After eight months of treatment he also expressed a wish to grow up. He was free from the intense fears. He was still sensitive, however, and was not entirely secure.

BEVERLY, Chicago.

A REJECTED CHILD. K. PENSIMUS, Psychoanalyt. Quart. **4**:37 (Jan.) 1935.

A case is reported of the cure of a severe problem child in kindergarten. A 4½ year old boy was poorly developed and poorly nourished and was a hated child living with his mother. A cousin of his own age, who lived in the home, received all the attention of several adults. The patient was constantly punished. In school he presented a food problem; he was of an aggressive, destructive, screaming, teasing type. With no rights at home, he found himself at school with equal rights. At school he received kindness and love from the teacher, which he never had at home. At first he had no confidence. For months he became more violent toward others and himself, which brought him to complete identifica-

tion with the cousin at home. During this time he had no confidence, scrubbing on his drawings, etc. In looking for the love he missed at home, he sucked his apron and clothing and finally put everything he could get hold of into his mouth, including food. When the identification with his cousin was accomplished, he was able to play and do the things the other children did. He developed self-confidence and became normal in behavior.

BEVERLY, Chicago.

PSYCHOANALYSIS AND THE FUTURE OF EDUCATION. ERIK HOMBURGER, Psychoanalyt. Quart. **4**:50 (Jan.) 1935.

The authors point out how psychoanalytic principles can and should be used by the teacher. The importance of allowing children to ask and have all questions answered is emphasized. Sexual curiosity is masqueraded as a desire for knowledge. The significance of rage and similar emotions should be taught to children.

BEVERLY, Chicago.

CHILD ANALYSIS AND THE MOTHER. DOROTHY T. BURLINGHAM, Psychoanalyt. Quart. **4**:69 (Jan.) 1935.

The mother is a great influence during analysis. She can be ignored; the child can be removed from the home, or her cooperation can be obtained. Cooperation can be had by showing interest in the mother as well as the child and by producing a sense of guilt that she had not done better. By means of cases the author points out the importance of the influence of the mother on the child during the analysis. The importance that the analyst keep unbiased his own conflicts and attitudes toward the mother and child was emphasized.

BEVERLY, Chicago.

PHOBIA IN A TWO AND A HALF YEAR OLD CHILD. BERTA BORNSTEIN, Psychoanalyt. Quart. **4**:93 (Jan.) 1935.

Severe anxiety developed in a girl, aged 2 years and 4 months. She refused to lie down in bed but slept sitting up. She was the only child. She was trained in cleanliness before the age of 1 year. The mother showed great pleasure in cleanliness. Prior to the onset of the anxiety the child was exposed to several sexual experiences—seeing a boy undressed, the grandfather urinate, the maid change menstrual pads, etc. The patient confused the mother's wishes for cleanliness with pleasure in defecation and the fear that she would be deprived of her mother and home. The mother had taken a trip, and the grandmother completed the toilet training by force and scaring. "It is characteristic for children at the anal sadistic level to respond with an anal reaction to sexual excitation from a genital source." The situation in this case was complicated, therefore, by seeing the grandfather urinate and by other experiences. The child recovered with treatment.

BEVERLY, Chicago.

FROM THE ANALYSIS OF A BEDWETTER. ANNY ANGEL, Psychoanalyt. Quart. **4**:120 (Jan.) 1935.

A 12 year old girl had wet the bed every night since the age of 3 years. At this time she was left by the parents with the grandmother. When they returned they found that she had been sick with severe vomiting. Through the analysis the girl reconstructed the experience which caused the difficulty. "A gypsy had lured her into his room where, at his request, she had exhibited her skill in turning somersaults, thereby exposing herself. She had interpreted his laughter as mockery. He had shown her his penis and had made her touch it and then had played with her genitalia. It was at this moment, she thought, that she had developed the idea that with so defective a genital it would be impossible to control her urine so that it must always flow out against her will." The enuresis stopped when these facts were brought out and explained.

BEVERLY, Chicago.

EXCERPT FROM THE ANALYSIS OF A DOG PHOBIA. EDITH STERBA, Psychoanalyt. Quart. **4**:135 (Jan.) 1935.

A 7½ year old girl was taken for treatment because of an extreme fear of dogs, which caused her to scream and tremble when she saw one. She refused to play outdoors and did not do school work, which she was able to do very well. The acute phobia developed after an attack of measles and infection of the ear, at which time she received an enema daily for six weeks. The origin of the phobia was traced to the mother's stern prohibition of masturbation at the age of 3 years, when the patient was threatened with being given away and was told masturbation would make her sick. At that time she was terribly scared by both her parents because she put her hand in the mouth of a playful police dog. The fear became acute after the enemas, which she enjoyed, which she was told would keep her from getting sick and which were connected with sexual acts, sex relations between the parents which had been observed and which the patient considered sadistic, possibly the cause of physical injury and very wrong. There was further criticism when the patient was caught doing these things with her sister. The child was cured by the analysis.

BEVERLY, Chicago.

EXHIBITIONISTIC ONANISM IN A TEN YEAR OLD BOY. EDITH BUXBAUM, Psychoanalyt. Quart. **4**:161 (Jan.) 1935.

A 10 year old boy had ticlike twitching movements, blinking of the eyes, etc. In addition, he masturbated excessively in an exhibitionistic manner. The purpose of the study was to see whether the ticlike movements, which were convulsive, could be influenced by an analysis as well as to clear up the exhibitionism. Through analysis the exhibitionism was cured, and the tics and convulsive movements became less frequent but still remained. The author emphasized that the possibility of organic factors must be considered. The treatment was broken off before it was finished.

BEVERLY, Chicago.

A CHILD ANALYSIS. STEFF BORNSTEIN, Psychoanalyt. Quart. **4**:190 (Jan.) 1935.

A detailed account is given of the psychoanalysis of a 3 year old boy, who was treated through play methods. The analysis required about one hundred hours of treatment. The author gives a detailed account of the important hourly conferences. The chief reason for the treatment was the patient's inability to pass the stool. He held back the stool because of an obvious anxiety. The case is important because it demonstrates the importance of an early traumatic experience in the later instinctual development.

BEVERLY, Chicago.

STATISTICAL STUDY OF HEREDITARY TAINT IN A SELECTED GROUP: SIBLINGS AND PARENTS OF 362 OFFICERS AND INMATES OF A HOSPITAL IN SAXONY. BERTHOLD BERLIT, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:622 (May) 1935.

Berlit reports a study in which an attempt was made to estimate the incidence of mental disease in a control group of patients. In order to evaluate the data collected in the study of the genetics of mental disease it is necessary to know the incidence of mental disease, personality and character defects, mental deficiency and epilepsy in control groups. The author chose the employees of a hospital for patients with mental disease as the control group because of their willingness to cooperate and their relative reliability concerning the incidence of mental disease in relatives. In estimating the incidence of a particular disease only those relatives were included who were within the age group during which that disease is known to occur. The frequency of psychopathy, for instance, was determined in those over 10 years of age and that of hysteria in those over 5.

In studying 1,807 siblings Berlit found the following percentages of incidence of various diseases: dementia paralytica, 0.41; schizophrenia, 0.79; epilepsy, 0.41; mental deficiency, 0.62; hysteria, 0.41; psychopathic personality, 2.4; psychopathy-like states, 4.8; alcoholism, 0.08; suicide (without psychosis), 4.6; mortality from tuberculosis, 24.1. One and thirteen hundredths per cent of the siblings had wandered away and were not located.

In 724 parents the following percentage incidence of abnormal mental states was found: schizophrenia, 0.15; manic-depressive psychosis, 0.47; dementia paralytica, 0.15; senile psychosis, 0.95; mental deficiency, 0.13; hysteria, 0.27; suicide, 1.3 (without psychosis); alcoholism, 0.41; psychopathy, 2.1; psychopathy-like states, 4.8; mortality from cerebral accidents, 17.3 (including parents between 21 and 100 years of age); mortality from carcinoma, 15.

Berlit realizes the limitations of the data he presents and urges other similar surveys. As more studies such as this are collected, the conclusions will necessarily become statistically more valid. An important source of error is the difficulty of being sure of the psychiatric diagnosis. The data collected from a group of this type are somewhat more accurate than similar information from a random sample of the population.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

DIAGNOSIS AND THERAPY OF MONGOLISM. ERICH STERN, Ztschr. f. Kinderh. **55**:372 (Sept.) 1933.

Stern treated eighteen patients with mongolism with a combination of endocrine products, roentgen radiation and a preparation which consists of iodine and a lipoid. He started the treatment with small doses of the last-mentioned preparation, and from two to three weeks later he added thyroid every other day. Later he added hypophysial extract and either testicular or ovarian extract. In addition, he used roentgen therapy.

The author excludes two of these cases from his series because the period of treatment was too short at the time the report was written. In seven of the sixteen cases no apparent improvement was shown. In two cases the result was questionable. In the other seven cases, however, there was marked improvement, particularly in speech, and increase in height and weight. The physiognomy of the children was also improved.

LEVINSON, Chicago.

Diseases of the Genito-Urinary Tract

THE URINARY CONCENTRATION IN DIABETES INSIPIDUS: A COMPARISON OF THE EFFECTS OF SEVERAL DRUGS. ELMER L. DEGOWIN, Am. J. M. Sc. **190**:747 (Dec.) 1935.

Two cases of diabetes insipidus of unknown etiology have been studied with reference to the effect of various drugs on the concentration of the urine.

A test has been devised which allows an evaluation and comparison of the effect of drugs on the urinary concentration. This test eliminates the factor of thirst from consideration.

These results supplement the studies of F. M. Smith and Vidgoff on the effects of the nasal insufflation of powdered posterior pituitary substance. In Smith's experiments the possibility of some effect of the drug on thirst was not eliminated. The tests confirm Eichhorst's report on the efficacy of antipyrine. The reports of Scherf and Kahn as to the value of aminopyrine are also confirmed. In view of the recent reports of the occurrence of agranulocytosis following the administration of aminopyrine, this drug should be used with caution.

HENSKE, Omaha.

FURTHER EVIDENCE FOR THE PRIMACY OF POLYURIA IN DIABETES INSIPIDUS. CURT P. RICHTER and JOHN F. ECKERT, Am. J. Physiol. **113**:578 (Nov.) 1935.

Polydipsia produced in fourteen rats by partial hypophysectomy was eliminated by ligation of the ureters. As has been shown previously, the polydipsia followed the polyuria which occurred immediately after the experimental production of diabetes insipidus.

NOURSE, Cleveland.

ANGIOMA OF THE KIDNEY: REPORT OF A CASE WITH AN ANALYSIS OF TWENTY-SIX PREVIOUSLY REPORTED CASES. R. H. JOCELYN and HAROLD BALME, Brit. J. Surg. **23**:282 (Oct.) 1935.

To date twenty-seven instances of angioma of the kidney have been collected. In 53 per cent of the cases hematuria appeared before the thirtieth year. In the majority of cases the bleeding was intermittent, the intervals between attacks lasting several years. In other cases there was profuse bleeding demanding immediate treatment. In eleven cases there was lumbar pain, which was usually colicky in nature. The angioma may appear in any part of the kidney, but in the majority of the cases reported it appeared to be a cavernous or capillary angioma situated immediately beneath the mucous membrane lining the pelvis or one of the calices of the kidney, rupturing through the latter and giving rise to hemorrhage. A differential diagnosis has to be made from hemorrhagic nephritis, tuberculosis, renal calculus, renal growth, hydronephrosis, purpura and renal varix. The treatment consists of pelvic lavage with silver nitrate or epinephrine hydrochloride, unless the bleeding cannot be controlled, in which even total or partial nephrectomy will have to be considered. A case observed by the authors which occurred in a 15 year old boy is cited.

SUMMERFELDT, Toronto, Canada.

THE EFFECTS OF OBSTRUCTION OF THE URINARY TRACT, WITH PARTICULAR RELATION TO THE FORMATION OF STONES. J. GRAY, Brit. J. Surg. **23**:451 (Oct.) 1935.

Series of rabbits with partial and complete unilateral urinary obstruction were investigated. The period of obstruction varied from two weeks to six months. In complete urinary obstruction there is no tendency to stone formation. In partial obstruction there is a marked tendency to stone formation, owing to an increased calcium content of the kidney and a pathologic condition of the pelvic epithelium, so that calcium may be deposited around this nucleus. In cases of obstruction there are a diminution of the blood supply, dilatation of the tubules and loss of function and pathologic changes in the epithelium of the pelvic mucosa.

SUMMERFELDT, Toronto, Canada.

CONGENITAL DILATATION OF THE URETER. CEDRIC HILLIARD, Brit. M. J. **2**:838 (Nov. 2) 1935.

A case of dilatation of the ureter is reported, with an account of the symptomatology and the operation.

ROYSTER, University, Va.

ANEPHROGENESIS. F. J. SAMBROOK GOWAR, J. Obst. & Gynaec. Brit. Emp. **42**:871 (Oct.) 1935.

Gowar reports a case of bilateral absence of the kidneys and ureters in an infant who died one hour after birth. There was a normal amount of amniotic fluid. After a discussion of the relation between the fetal urinary output and the amount of amniotic fluid, the conclusion is reached that the fetal urine may augment the amount of amniotic fluid but is not the primary source of it.

ADAIR and POTTER, Chicago.

AZOTEMIA IN ACUTE BRIGHT'S DISEASE. J. BASIL RENNIE, Lancet **2**:658 (Sept. 21) 1935.

This study is based on the observation of ninety-eight children with acute nephritis. Azotemia was found in 60 per cent of those examined within seven days of the onset and in 51 per cent of those first examined during the second week. The nonprotein nitrogen content of the blood bore no relation to the incidence or severity of the cerebral manifestations in acute nephritis. Persistence of the azotemia after the third week is of grave significance.

LANGMANN, New York.

SOME ASPECTS OF ACUTE NEPHRITIS IN CHILDREN. M. COCKBURN, M. J. Australia **2**:643 (Nov. 9) 1935.

Cockburn reports the results of a study of one hundred and forty-six cases of acute nephritis, including cases of the acute focal form and those of the acute diffuse form. Following a brief review of the history and the development of the present knowledge of the disease, the clinical symptoms and signs are discussed. The author reviews the literature pertaining to the etiology. From the study of his own series he found that acute tonsillitis was the precursor of the disease in 30 per cent of the cases; scarlet fever in 9.8 per cent; infection of the skin, consisting mainly of impetigo contagiosa, in 8.6 per cent; bronchopneumonia in 0.75 per cent, and various unknown factors in 26 per cent. The disease showed the highest incidence in Adelaide, Australia, in the damp cold fall season.

Operations for removal of foci of infection, such as tonsillectomy, antrostomy on the maxillary antrum and mastoidotomy, had no bearing on the end-results in these cases. In 28 per cent of the patients operated on relapse occurred. However, relapse did not prolong the average course of the illness. Cockburn concludes that the prognosis for complete recovery in acute nephritis is very good and that there is no difference in the end-result in patients subjected to operative removal of septic foci and in those who are not subjected to operation.

GONCE, Madison, Wis.

VESICAL CALCULUS. ANDRÉ MARTIN and PAUL AIMÉ, Bull. Soc. de pédiat. de Paris **32**:350 (June) 1934.

A boy, 10 years old, had pain in the iliac fossa for about half an hour six months prior to examination. There was no hematuria or history of renal colic. Since this time he had had repeated attacks of balanitis and, for the past month, severe pain in the penis and frequency of urination. The urine showed numerous leukocytes and bladder cells, but no micro-organisms. Roentgenographic examination revealed a large stone in the bladder. A suprapubic cystostomy was performed, and the stone was removed. A retention catheter, inserted at operation, was in place for fourteen days. The child had fever for a few days after operation, and the incision of the skin partially broke down, but complete recovery followed. The calculus weighed 14.5 Gm. and was ovoid and yellowish. Chemical examination revealed no uric acid but a large amount of cystine crystals. The stone was soft and was easily cut with a knife. It was soluble in hydrochloric acid, sodium hydroxide and ammonia, but not in acetic acid. After combustion little ash remained. The condition is by no means as frequent among children in France as reports indicate it to be in the Orient, but its possibility should be borne in mind.

BENJAMIN, Montreal, Canada.

FAMILIAL LIPOID NEPHROSIS: REMARKS ON PATHOGENESIS. G. BLECHMANN, Bull. Soc. de pédiat. de Paris **32**:362 (June) 1934.

Two cases, one occurring a few years after the other, of lipoid nephrosis are described, which developed after infection of the throat in children of the same family. The first child died; the second was treated with thyroxine and a diet

high in proteins and recovered. The first child had a negative Wassermann reaction, and the second child a slightly positive reaction; so he was given lactate of mercury and was treated for nephrosis. Later, the Wassermann reaction was negative. The cases are cited of two children with lipoid nephrosis in one family, reported by Volhard, to add evidence to the observation that the condition may be familial. It is considered that hereditary syphilis is an etiologic factor in the development of this disease in that it supplies the unhealthy soil for the metabolic and endocrine disturbances. Persons who discussed the paper were not at all in agreement with this theory.

BENJAMIN, Montreal, Canada.

ESSENTIAL ENURESIS AND LUMBOSACRAL MALFORMATION. P. R. BIZE, Bull. Soc. de pédiat. de Paris **32**:607 (Dec.) 1934.

Enuresis was associated with spina bifida occulta in a number of children in approximately the same proportion in which the latter condition was observed in a group of children who did not have enuresis. In cases of true spina bifida with cystic tumor, enuresis may result from involvement of the cord. Patients with spina bifida revealed by roentgenographic examination were treated medically and surgically. Because of the tendency of enuresis to disappear as the child grows older and the recognized importance of certain psychic factors in relation to this condition, it is emphasized that one cannot ascribe success in the treatment of this condition to the particular medical or surgical therapeutic procedure employed.

BENJAMIN, Montreal, Canada.

RACHISCHISIS AND NOCTURNAL URINARY INCONTINENCE. E. LESNÉ, J. A. LIÈVRE and MME. J. A. LIÈVRE. Bull. Soc. de pédiat. de Paris **32**:613 (Dec.) 1934.

Forty-one children from 7 to 14 years old who had nocturnal enuresis and in whom no physical defects were found were examined roentgenologically for evidence of spina bifida occulta. Twenty-eight of these showed incomplete development of the vertebral arch. A control group of children without nocturnal enuresis showed this condition in approximately the same percentage of cases. The conclusion reached is that no significance is to be attached to the finding of spina bifida in children with nocturnal enuresis.

BENJAMIN, Montreal, Canada.

VULVOVAGINITIS OF SMALL GIRLS. GRÉGOIRE CHICK, Progrès méd., Dec. 7, 1935, p. 1954.

In order to lessen the chances of error in diagnosing gonorrheal vaginitis in small girls, the author uses the method of culture of Levinthal (an agar plate with 20 per cent ascitic fluid in a mixture of agar and blood) and stains by the method of Van Loghem and Gram. He feels that gonorrheal vaginitis in these patients is almost always acute. Other acute forms of vaginitis are those due to Streptococcus haemolyticus, which usually occur with scarlet fever, and those due to the influenza bacillus and to the diphtheria bacillus. The chronic forms may be secondary to malnutrition or caused by a foreign body or by infection with oxyuris.

LESLIE, Evanston, Ill.

RETICULOCYTES IN PAROXYSMAL HEMOGLOBINURIA. M. KASAHARA, T. TSUDA and M. NAGAHAMA, Ztschr. f. Kinderh. **55**:479, 1933.

The studies of Kasahara, Tsuda and Nagahama show that the number of reticulocytes is increased in paroxysmal hemoglobinuria, particularly during and following the attacks. The increase of the reticulocytes in this disease, the authors believe, is due to a degenerative process and not entirely to a regenerative process of the blood.

LEVINSON, Chicago.

COLIC DUE TO RENAL CALCULUS IN EARLY CHILDHOOD. WALTER BEHRENS, Ztschr. f. Kinderh. **55**:637, 1933.

Behrens reports a case of urinary calculi in a boy 3½ months old.

LEVINSON, Chicago.

THE XANTHOPROTEIC REACTION IN BLOOD AS A TEST OF RENAL FUNCTION. HÅKON RASMUSSEN, Acta med. Scandinav. **86**:302, 1935.

Rasmussen found that the xanthoproteic reaction (X. R.) is not an early sign of renal impairment. It becomes positive in chronic nephritis when the uremic coma is imminent. In the uremic state of acute nephritis there may be a normal reaction. The test is useful in the differentiation of uremia from cardiac decompensation and hypertensive encephalopathy, because in these conditions there is no positive reaction, in spite of the increased urea content of the blood. Some increase in the xanthoproteic reaction may occur in dehydration or diabetic coma. False high values are obtained if the patient receives salicylates.

KAJDI, Baltimore.

Diseases of the Ductless Glands; Endocrinology

LINGUAL THYREOID GLAND IN A CRETIN OF SEVENTY-EIGHT YEARS. TUDOR JONES, Anat. Rec. **63**:315 (Nov.) 1935.

Complete absence of the thyroid was noted in the cervical region but a mass the size of a hazel-nut was observed near the base of the tongue.

SNELLING, Toronto, Canada.

FURTHER STUDIES ON THE THYMUS AND PINEAL GLANDS. L. G. ROWNTREE, J. H. CLARK, A. STEINBERG, A. M. HANSON, N. H. EINHORN and W. A. SHANNON, Ann. Int. Med. **9**:359 (Oct.) 1935.

This article includes observations on the sixth to the tenth generation of rats which had received daily injections of thymus extract. The results of the study of the first five generations of rats so treated was published in July 1934. In addition, the effect of thymectomy in successive generations of rats and further studies on the effect of injections of extract of pineal gland in rats is discussed.

Results similar to those found in the first five generations of rats treated with thymus extract were noted in the next five generations, except that in each subsequent generation there was an increase in precociousness, a maximum being reached in the tenth generation. The psychic precocity was as striking as the physical in the strain of rats treated with thymus extract. These animals were healthy, contented and docile, and their actions resembled in every way those of normal controls.

The effect of thymectomy in successive generations of parent rats on the growth and development of the young showed that growth was retarded during the first ten weeks of life to the extent of from 25 to 30 per cent, but after maturity the curves for weight of these animals were essentially normal.

The same technic used in the rats treated with thymus extract was employed in a group of animals treated with an extract of pineal gland. This substance was administered continuously to successive generations of parent rats. Suitable controls were used, as in the previous studies. To date five generations of the strain of rats treated with extract of pineal gland have been under observation. In the first generation no effect was noted other than a moderate loss of weight, evidence of sexual excitation or increased size of the penis and early breeding. In the second generation there was definite retardation of growth, with mild precocity in gonadal development. In subsequent generations there was increasing retardation of growth, with accruing acceleration in gonadal bodily development. These observations should not necessarily be taken to mean that a function of the pineal

gland is to retard growth and accelerate differentiation, since experiments under way indicate that pinealectomy also retards growth and is associated with accelerated development.

Other biologic effects noted in these animals treated with extract of pineal gland are those relating to activity, behaviorism, the time of weaning and, frequently, blindness.

READING, Galveston, Texas.

TUMORS IN THE REGION OF THE PINEAL BODY. HOWARD ZEITLIN, Arch. Neurol. & Psychiat. **34**:567 (Sept.) 1935.

Three cases of tumor arising in the region of the pineal gland—a teratoma, an astroblastoma and a meningioma—are reported. In addition to the general symptoms of increasing intracranial pressure, the important localizing symptoms of tumor in this region are loss of conjugate movement upward of the eyes above the horizontal plane and dilated pupils with loss of the pupillary light reflex, due to pressure on the quadrigeminal plate, which affects the nuclei of some ocular muscles and the tracts in the corpora quadrigemina.

BEVERLY, Chicago.

A PITUITARY SYNDROME. MAX M. GOLDBERG, Arch. Neurol. & Psychiat. **34**:631 (Sept.) 1935.

Goldberg reports the case of a 12 year old girl with a history of rapid growth from 5 to 8 years of age and with the complaint of weakness, nervousness, crying easily, trembling spells (especially before and after menstruation), overweight and overdevelopment. The condition resembled the basophilic syndrome of the pituitary gland first reported by Cushing, except that there were probably acidophilic changes going on at the same time.

BEVERLY, Chicago.

AN ATYPICAL FAMILIAL ENDOCRINOPATHY IN MALES WITH A SYNDROME OF OTHER DEFECTS. WILLIAM ANTHONY REILLY, Endocrinology **19**:639 (Nov.-Dec.) 1935.

Two cases of an atypical familial endocrinopathy are reported, which occurred in brothers aged 19 and 6½ years. Few reports of similar cases could be found in a search of the literature, but some which had many features in common with these have been reported under the names Morquio's disease, the Helmholtz-Harrington syndrome and pleonosteosis.

The characteristics of the syndrome, as seen in the two cases reported are: familial occurrence in males of a typical physical development, having almost identical facies (resembling the appearance in hypothyroidism); optic neuritis; a normal mentality; limited extension of joints which are always partially flexed; thick, pudgy extremities; thick bones; retarded development of the epiphyses; dry, thick, coarse hair and cutaneous areas (on the extremities, particularly); enlargement of the abdomen because of hepatosplenomegaly, and a tendency toward lymphocytic leukopenia. There was no improvement under thyroid therapy.

In one patient who came to autopsy areas of degeneration and necrosis were seen in the anterior lobe of the pituitary. The thyroid showed a picture of combined mild hyperplasia and increase of interlobular connective tissue, with evidences of degeneration in many of the alveolar cells. The thymus was enlarged.

JACOBSEN, Buffalo.

THYROID CARCINOMA WITH METASTASIS IN THE CILIARY BODY. H. C. ORR and I. L. JOHNSTONE, Brit. J. Ophth. **19**:593 (Nov.) 1935.

The patient was a coal miner 16 years of age. There was clinical evidence of a tumor of the ciliary body on the temporal side of the eyeball. The pathologic examination of the excised eye showed the outer two thirds to be occupied by a

carcinomatous mass. The cells composing the growth were columnar and formed multiple papillae. In the majority of the papillae the central core was slender, often edematous, and consisted of young fibrous tissue with new-formed blood vessels. Fine pigment was scattered throughout the growth. In one of the papillae the columnar cells appeared to be continuous with the outer layer of cells covering the normal ciliary processes. In the choroid immediately behind the growth were massive hemorrhages. In the thyroid area of the neck there was a hard fixed lump which had been present for at least eight years. The growth was removed and found to be a columnar cell carcinoma.

Orr and Johnstone believe the condition to be rare if not unique.

The article is illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

TUMORS OF THE HYPOPHYSIS: THEIR EARLY DIAGNOSIS AND THERAPY. P. PUECH, Ann. de thérap. biol. **1**:1 (Oct. 15) 1934.

This article includes a general survey of the field of tumors of the hypophysis and of its vicinity. There is a separation of the glandular tumors, the craniopharyngiomas, the lesions developing in the same neighborhood and other pathologic processes that may be confused with the preceding. Puech lays particular stress on the mild endocrine disorders observed in cases of chromophobe adenoma and their rather satisfactory remission following roentgen therapy. However, the diagnosis is usually made in such cases from the disturbances in the visual fields, which occur only after the tumor has outgrown the sella turcica. After the tumor has grown to a large size it may produce various symptoms, depending on the direction of its spread. The acidophilic adenomas are usually easy to diagnose on account of the pronounced acromegalic changes, and ocular symptoms are much less common. However, in cases of transitional adenoma more serious results may be expected owing to pressure on the optic nerve and other parts.

The craniopharyngiomas may develop above, within or below the sella turcica and are more likely to give rise to indications of intracranial hypertension, to disturbance of hypothalamic function and particularly to hypophysial dysfunction, together with signs of pressure on the chiasm which are often striking. A surprising number of these tumors and cysts are revealed in roentgenograms, owing to their frequent calcification. Differential diagnosis between these two types of tumor and meningioma of the tubercle of the sella turcica or glioma of the optic chiasm may be difficult. The meningioma of the olfactory nerve and the meningioma arising from the lesser wing of the sphenoid bone are usually more easily diagnosed, but sometimes a tumor situated at a distance from the hypophysis may cause disturbances in the function of the gland. The usual effect of arachnoiditis about the chiasm is to produce visual disturbances of irregular type without a definite effect on the hypophysis itself. Infection of the sinuses in the genesis of such arachnoiditis seems to be common.

FREEMAN, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.]

BENEFICIAL EFFECT OF ANTERIOR PITUITARY EXTRACT IN THE CASE OF A DIABETIC CHILD. M. A. BRETON, J. de méd. de Paris **55**:852 (Sept. 26) 1935.

Breton reports that the daily administration of an anterior pituitary extract by mouth to a girl 10 years of age, given originally because of retarded growth, caused amelioration of diabetes, which had been present for four years.

LESLIE, Evanston, Ill.

SALIVARY GLAND INCLUSION IN THE HYPOPHYSIS. E. V. MÂRZA and V. D. MÂRZA, Rev. franç. d'endocrinol. **12**:479 (Dec.) 1934.

The authors report a rare case of inclusion of salivary gland tissue in the hypophysis. Only two other similar cases are on record, one reported by Bevaqua

in 1911 and the other by Oberling in 1924. The case studied by the authors is that of a girl, aged 18, who died as the result of rupture of the spleen caused by an accident. Of great interest were two small lobules of salivary gland tissue in the posterior lobe of the hypophysis. Each lobule had an excretory duct, which communicated with the large cyst in the intermediary lobe. Each salivary lobule was composed of about thirty or forty serous acini and only one mucous acinus. They were spherical or elongated, with a narrow lumen and a visible membrana limitans externa; in transverse sections they measured from 30 to 50 microns. The microscopic appearance of the cells was that of normal active salivary cells. Each lobule had its own excretory canal; they all opened into one common duct which communicated with the cyst in the intermediary lobe. The authors believe that the salivary gland inclusions in the hypophysis are probably aberrant shoots carried along with Rathke's diverticulum into the infundibular region.

NOTKIN, Poughkeepsie, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

DI-IODO-TYROSINE COMPARED TO COMPOUND SOLUTION OF IODINE, U. S. P. B. BÜSSEMAKER and A. POLLMANN, Monatschr. f. Kinderh. **63**:422, 1935.

Di-iodo-tyrosine has been recommended as an antagonist to thyroid secretion. To determine whether this substance is specific or whether the effect is due to its iodine content Büssemaker and Pollmann studied its effect on the excretion of creatine as compared with the effect of compound solution of iodine, U. S. P. Feeding thyroid extract leads to an increased excretion of creatine. Both di-iodo-tyrosine and compound solution of iodine, U. S. P., neutralized this effect. The authors conclude that the action of di-iodo-tyrosine is due simply to its iodine content.

GERSTLEY, Chicago.

OBSERVATIONS ON INSULIN-ADRENALIN TREATMENT BY THE CLAUSEN METHOD. T. THUNE ANDERSEN, Acta med. Scandinav. **86**:361, 1935.

Andersen treated seventeen patients with diabetes mellitus with epinephrine added to insulin. None of the patients became worse. Thirteen showed improvement, and in seven of these the glycosuria disappeared or significantly diminished. Those patients who had previously shown hypoglycemic symptoms became free from them.

KAJDI, Baltimore.

Diseases of the Muscles, Bones, Joints and Lymph Glands

ROENTGEN TREATMENT OF LYMPHOBLASTOMA (HODGKIN'S DISEASE). KENNETH R. MCALPIN and ROSS GOLDEN, Am. J. Roentgenol. **29**:83 (Jan.) 1933.

The author treated forty-six patients by means of irradiation of the superficial nodes. Usually from one half to two thirds of the erythema dose of medium voltage radiation with a 3 mm. filter of aluminum was repeated at intervals of two weeks. The mediastinal and abdominal nodes were irradiated with 200 kilovolts through a 0.5 mm. filter of copper and a 1 mm. filter of aluminum at an anode distance of 50 cm. from the skin. Usually from one eighth to one twelfth of the erythema dose was used at one sitting and was repeated at first at intervals of from two to four days and later at longer intervals. Fever was considered to be a contraindication to irradiation. Roentgen therapy is indicated in Hodgkin's disease, and as a rule the smaller dose at frequent intervals produces the best results. While the authors are willing to admit that Hodgkin's disease is incurable, they feel justified in maintaining that some patients do surprisingly well with the treatment—so well that it is possible that death is due to other causes. "We do no expect to cure, but hope to make life not only longer but happier."

STULIK, Chicago.

DESTRUCTION OF EPIPHYSES BY FREEZING. R. B. BENNETT and W. P. BLOUNT, J. A. M. A. **105**:661 (Aug. 31) 1935.

The authors report a case of stunted growth of the fingers resulting from freezing in an 8 year old girl. They state that they have been able to find only one other report of such a condition. In both instances the onset appeared six months after freezing.

BONAR, Salt Lake City.

OSTEOMYELITIS IN INFANTS. RICHARD E. DILLEHUNT, Surg., Gynec. & Obst. **61**:96 (July) 1935.

Basing his opinion on experience with more than three hundred cases of subacute and chronic osteomyelitis, Dillehunt states the belief that osteomyelitis causes as great morbidity and crippling as do tuberculosis of the joints and infantile paralysis.

Error in the diagnosis is due to the rarity of the disease in individual practice, to the absence of objective phenomena and to the negative roentgen findings at the onset. "If a child under 13 years of age is seized with pain in an extremity, and he shows loss of function, elevation of temperature, and leucocytosis, that child has acute osteomyelitis. . . . In such a picture the obligation of the doctor is to determine the point of localized tenderness over the end of a long bone, and upon recognition of the point of tenderness, to open the cortex and drain."

Acute osteomyelitis is a disease of children because it is a hematogenous infection lodging in epiphysial end-arteries and venous sinuses which do not exist in bone in adults. The adult form of osteomyelitis is apparently a lighting up of an old quiescent process acquired in childhood. Conditions for the development of the process are most favorable between 5 and 11 years of age.

Among the points relating to the diagnosis the following are emphasized:

Boils are the most frequent primary focus, otitis media the next most frequent. The onset is abrupt, usually with involvement of an extremity and without sufficient etiologic evidence to explain the findings. Pain is constant and is not relieved by rest to the degree obtaining in a lesion of a joint. Loss of function is without muscular spasm, as in a lesion of a joint, the extremity lying limply as in poliomyelitis. An infected joint cannot be moved without pain. A joint seemingly but not really the seat of infection and near a focus of osteomyelitis can be moved carefully without pain.

Tenderness in osteomyelitis, in distinction from that in articular involvement, is at the diaphysial side of the epiphysial cartilage.

Swelling, heat, redness and roentgen evidence may all be lacking in the presence of actual osseous changes, which are undiscernible early.

Few cases have been reported in infants. Three cases in patients under 6 months of age, including two in patients under 6 weeks of age, are described, with accompanying roentgenograms. In all three cases osseous foci were surgically drained. Culture of the fluid was negative in one case, showed Staphylococcus aureus in one case and gave a growth of short chain streptococci in the third instance.

Dillehunt concludes that acute osteomyelitis is rarely diagnosed with sufficient promptness. It is rare in infants, in whom it is more benign than in adults, notwithstanding the fact that loss of function is regularly manifest in infants with this disease. Foci may become sterile spontaneously and undergo spontaneous resolution. Sequestrums do not form. Drainage alone seems adequate treatment, and the prognosis for affected infants is favorable.

GRAVES, New York.

RHEUMATOID ARTHRITIS: ITS ETIOLOGY AND TREATMENT BY DIATHERMY. C. A. ROBINSON, Brit. J. Phys. Med. **10**:58 (Aug.) 1935.

The author expresses the belief that in a vast majority of cases rheumatoid arthritis in women is due to infection of the cervix and in men to infection of

the prostate. He reports good results with the use of intravaginal and intrarectal diathermy. He claims to have successfully treated Still's disease in children in this manner.

HARTMAN, Cleveland.

LYMPHOGRANULOMATOSIS IN A CHILD. L. BABONNEIX and JOURDAN, Bull. Soc. de pédiat. de Paris **32**:573 (Dec.) 1934.

A boy, aged 13½ years, was at first thought to be suffering from tuberculous adenitis. The swelling of the glands did not subside, so biopsy of a cervical node was performed. This revealed the condition to be lymphogranulomatosis. All the glands were excised which could be dissected on the side of the neck on which the specimen had been taken for biopsy. Six months later only slight general adenopathy could be detected on physical examination, but a roentgenogram of the chest showed a huge mass at the right hilus. Roentgen therapy was followed by diminution in the size of this mass. The reaction to tuberculin was negative, which tends to disprove the theory that this disease is related to tuberculosis.

BENJAMIN, Montreal, Canada.

SEVERE OSTEO-ARTICULAR DYSTROPHY IN A GIRL OF TWELVE YEARS. M. APERT, R. LIÈGE and J. DENET, Bull. Soc. de pédiat. de Paris **32**:577 (Dec.) 1934.

A girl of 12 years presented marked osseous deformities so that she could not walk. The first deformity noticed was kyphosis at the age of 15 days. She had begun to walk when 2 years old, and at about 3 the deformities of the lower extremities became noticeable and gradually increased. She was able to hobble about with the aid of crutches until she was 10 years old. The head was large and square; the thorax was pointed anteriorly; there was dorsolumbar kyphoscoliosis; the lower extremities were markedly shortened and curved and were flexed at the knees and hips; the feet were rotated internally, more markedly on the left than on the right; the upper extremities were curved and shortened, and extension was limited at the elbows, owing to the bony deformities, and the hands suggested the *main en trident* characteristic of achondroplasia. A number of roentgenograms are reproduced to show the marked osseous deformities, which involved chiefly the spine and the ends of the long bones. There was marked hypercalcemia. The condition was obviously not due to rickets or osteomalacia; it resembled in some respects dyschondroplasia described by Ollier, as well as the dystrophy of familial occurrence described by Morquio. In the former disease, however, the deformity is usually limited to, or at least much severer on, one side, and the spine is not affected. It is against the probability of Morquio's disease that the other children in this case were normal and that spinal deformity is a late manifestation. There was no enchondroma in this case.

BENJAMIN, Montreal, Canada.

GENERALIZED MUSCULAR HYPERTROPHY IN A YOUNG CHILD. ROBERT DEBRÉ and GEORGES SÉMELAIGNE, Bull. Soc. de pédiat. de Paris **32**:699 (Dec.) 1934.

A girl, 2 years old, had marked hypertrophy and hypertonicity of all the muscles of the body. She showed marked delay in ossification and dentition and poor mental development. The smooth muscles were apparently not affected. She was extremely short and very emaciated. She was given thyroid extract by mouth. After six months of this treatment the muscular hypertrophy disappeared, and all the defects improved remarkably; her mentality improved somewhat but far less than her physical condition. Although this condition, consisting of congenital muscular hypertrophy with extrapyramidal disturbances and mental deficiency, has been reported as being due to anaplasia of the corpus striatum and porencephaly, which were observed in a patient who came to necropsy, it is considered that some endocrine derangement referable to the thyroid plays a fundamental rôle.

BENJAMIN, Montreal, Canada.

OSTEOMALACIA AND TUBERCULOSIS. H. ESCHBACH, Bull. Soc. de pédiat. de Paris **33**:63 (Jan.) 1935.

A boy of almost 3 years had rickets and tuberculosis. His condition became rapidly worse, and he showed marked osseous deformity. Roentgenographic examination showed these conditions, as well as severe decalcification and advanced pulmonary lesions. He had received two doses of BCG in infancy. No autopsy was performed.

BENJAMIN, Montreal, Canada.

ACUTE OSTEOMYELITIS OF THE CLAVICLE; TOTAL SUBPERIOSTEAL RESECTION, WITH COMPLETE REGENERATION. RENÉ FONTAINE and RENÉ MAITRE, Rev. d'orthop. **22**:339 (July) 1935.

Fontaine and Maitre report a case of acute osteomyelitis of the right clavicle. Total subperiosteal resection was done, with complete regeneration of the bone. The final functional results were excellent.

RYAN, Vancouver, Canada.

CHRONIC CERVICAL ADENOPATHY. P. ROCA PUIG, Paidoterapia **14**:317 (Aug.) 1935.

The frequency and causes of chronic cervical adenopathy in children are briefly reviewed, and the treatment is given. In eleven of fourteen cases of scrofulous adenopathy treatment with iodine gave the best results; 1 cc. of a solution of iodine (0.03 Gm. of iodine) was injected intravenously or intramuscularly at intervals of from three to six days.

HERRON, Spokane, Wash.

CONGENITAL ARTHRODYSTROPHY. JOSÉ MORALES DIAZ, Pediatría españ. **24**:229 (July) 1935.

The author describes two cases of this rare disorder, first described by the late noted Latin-American pediatrician Luis Morquio. The subjects were sisters, 5 and 7 years old, who presented in a striking fashion the characteristic symptoms: dwarfing, short and narrow thorax and delayed ossification of the epiphyses. The author favors the theory that pluriglandular dysfunction is principally at fault in this disorder and that the thyroid, hypophysis and sex glands are chiefly concerned.

SCHLUTZ, Chicago.

CONGENITAL MELANOCARCINOMA OF THE MAXILLA. ANDOR DUDITS and BARNABAS SZABÓ, Monatschr. f. Kinderh. **63**:294, 1935.

A 6 month old infant was brought to the hospital suffering from neoplasm of the upper jaw, which first appeared on the seventh day of life, as a swelling the size of a pea. When the child was 5 weeks old the tumor had increased to the size of a nut, and from it a tooth was growing. Operation revealed that the infiltration was so extensive that the tumor could not be removed by radical surgical intervention. Ten roentgen treatments were given, and the child, now 9 months old, is still in good health. Three photomicrographs of the tumor are shown. The diagnosis is melanocarcinoma.

GERSTLEY, Chicago.

FAMILIAL OSTEOPSATHYROSIS IDIOPATHICA. T. HALBERTSMA and W. MOL, Maandschr. v. kindergeneesk. **4**:433 (Aug.) 1935.

Four children born of healthy parents are described. In the first-born child, who died several hours after birth, the condition was probably osteogenesis imperfecta. The next two boys were suffering from osteopsathyrosis, the elder having the more severe condition, and both presented *crâne à rebord*. There was no blueness of the sclera or deafness. The calcium content of the blood was normal and the phosphorus content somewhat increased. Examination of the calcium content of the bones showed diminution in the distal part of the radius in both

cases. The fourth child was normal in every respect. Osteogenesis imperfecta and osteopsathyrosis are considered to be two forms of the same disease, of which osteogenesis is the more severe and arises early in life and osteopsathyrosis manifests itself later.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

MALNUTRITION IN RELATION TO ULCERATION OF THE CORNEA IN GONORRHEAL OPHTHALMIA NEONATORUM. C. E. WALKER JR., Am. J. Ophth. **17**:1146 (Dec.) 1934.

Walker reviewed all cases of corneal ulcer in infants treated at the Massachusetts Eye and Ear Infirmary during the years from 1923 to 1933, inclusive, and a series of one hundred consecutive cases (1927-1928) in which smears were positive for gonococci. Particular regard was paid to health, weight, prematurity and gastrointestinal disturbances. He states the following conclusions:

"1. Aside from the accepted local treatment, careful attention should be directed toward the dietary regulation of patients with ophthalmia neonatorum.

"2. Premature infants seem to be more susceptible to corneal ulcers than full-term babies.

"3. Gain in weight seems to be inversely proportioned to corneal involvement and progress in the infant."

REESE, Philadelphia. [ARCH. OPHTH.]

THE OCCURRENCE OF CILIARY PROCESSES ON THE IRIS. A. B. REESE, Am. J. Ophth. **18**:6 (Jan.) 1935.

Reese finds that not infrequently one or all the fully developed ciliary processes may arise from the posterior surface of the iris instead of from their usual sites on the zona ciliaris. They differ from those arising from the ciliary body by being covered with a double layer of pigmented epithelium at their base, at which point the dilator muscle is interrupted. There is usually a bridge between the iris and the processes of the ciliary body, beneath which may be a recess having the appearance of a cyst. These processes in the iris may cause a congenital irregularity of the pupil, or their excision may cause undue reaction and even result in sympathetic ophthalmia.

REESE, Philadelphia. [ARCH. OPHTH.]

CONGENITAL RETINAL FOLD. I. MANN, Brit. J. Ophth. **19**:641 (Dec.) 1935.

Mann states that since 1928 six cases of this anomaly (in eight eyes) have come to her notice and that Weve has collected six instances to be reported. The failure of previous observers to recognize the condition was due to the fact that it bears some resemblance to persistent hyaloid artery and other forms of pseudoglioma. The eyes which she was able to examine microscopically had been excised because glioma was suspected.

The abnormalities belong to a group of defects in the gross structure and differentiation of the inner layer of the optic cup. They arise mostly after the 13 mm. stage of the embryo (when the cleft is closed), and in most cases the changes do not involve the region of the cleft and so do not fall into the class of colobomas. In a few cases the change may begin during the process of closure, so that orientation by means of the cleft is possible, but still the changes are not those of coloboma. In all the cases the condition is characterized by the appearance of a fold or ridge involving the inner layer of the optic cup and projecting into the vitreous. In some cases this fold is shallow; in others, high and sharp, with a falciform edge. Fine gradations occur, and when a series is studied it becomes evident that the deformity links up, on the one hand, with abnormalities of the region of the cleft and, on the other, with a group containing proliferations

of the inner layer with rosette and ridge formation and the congenital detachments found in microphthalmic eyes. However, the defects described constitute a definite group to which the term "congenital retinal fold" should be applied.

The ophthalmoscopic appearance of one of the eyes is described: The general level of the fundus could be seen only with minus lenses, and running from the disk outward in the horizontal meridian toward the temporal edge of the lens was a thick rolled edge visible with a + 12 diopter sphere (with retinal vessels on it), breaking up anteriorly into many strands attached to the ora serrata on the temporal side in the horizontal meridian. This ridge could have no connection with the fissure. The solid appearance of the fold, the septum-like connection with the retina, the presence of branches of the retinal artery on the fold and the attachment anteriorly to the ora serrata, with strands passing to the lens near the equator, are characteristic. The vitreous and the lens were clear; the eye, of normal size. In all cases strands of persistent embryonic vessels, either the main hyaloid artery or some of its branches, were adherent to the surface of the fold (not contained within the substance) and sometimes were seen with the ophthalmoscope but more often on microscopic examination only.

The situation of the fold is interesting. In most of the cases (Weve and Ancona) it occupied the lower temporal quadrant of the retina, passing from the disk downward and outward. In cases in which the condition was symmetrical but by no means in all cases did it run downward and outward.

The macroscopic appearance of several of the affected eyes is pictured and described.

Microscopic examination showed the condition to be a double fold of the retina pulled inward and attached to a persistent hyaloid artery. The inner layer of the optic cup was alone involved in the fold, the pigmented epithelium being unaffected. The retinal layers were somewhat disturbed, being puckered and distorted with some atypical rosette formation and hypoplasia (imperfect differentiation) of layers. The fold was vascularized by branches of the arteria centralis retinae which had grown into it from the disk. Adherent to its surface were branches of the hyaloid artery.

Embryologically speaking, the defect consists of the adhesion of the primary vitreous and its contents to one portion of the inner layer of the optic cup, the secondary vitreous which should normally separate them being absent along the line of adhesion. Secondarily to this adhesion both the structures involved become displaced, the inner layer of the cup being detached (or rather prevented from coapting with the outer layer) and raised up into a ridge, and the contents of the primary vitreous becoming displaced from the optic axis toward the side of the adhesion.

In many of Weve's cases there was a familial and hereditary factor, and in cases in which the condition was bilateral the appearance was symmetrical, both of which facts are against any theory of fetal inflammation or fortuitous hemorrhage.

The article, which is a model of scientific presentation, is fully and beautifully illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

EXOPHTHALMOS FROM AN ORBITAL TUMOR. J. L. DEHOGUES, Ann. d'ocul. **172**:907 (Nov.) 1935.

Exophthalmos due to a tumor of the orbit or to a tumor that has developed in this area is fairly frequently noted in the literature. The subject is of considerable interest to oculists not only from the point of view of pathogenesis but also from that of the odd histologic picture which is at times revealed.

B. C., a colored youth 16 years of age, presented himself in February 1930 with severe exophthalmos of the right eye. Movements of the ocular globe were impossible, and this was found to be due to a hard tumor which was felt in the orbit and was found to be strongly adherent to the globe. The history extended

back over a period of three or four years. There was complete atrophy of the optic nerve, from which the patient had complete loss of vision. The details of the operation and of the histologic examination are given.

The existence of blastomas of the optic nerve developing on the oligodendric elements was reported by Hortega in 1932, who described three cases.

McKee, Montreal, Canada. [Arch. Ophth.]

A Previously Undescribed Malformation of the Palpebral Fissure, Conjunctiva and Cornea. G. Bietti, Boll. d'ocul. **17**:1537 (Dec.) 1934.

A baby girl 4 days old was seen who was normal except for the ocular deformities to be described. The eyelids were present, though the upper lids were smaller than normal. They were held widely apart by a fold of skin, with which the upper borders of the lid were fused directly, while below, under the fold of skin, shallow culdesacs were present. The folds of skin covered the globes except for a small part of each cornea, which was exposed. The corneas were small and xerotic, and the interior of the globes could not be seen through them. Bietti supposes that the adhesion between the borders of the lid which usually occurs was interfered with in some way, which prevented the normal development of the conjunctiva and cornea, the former being largely replaced by skin. Possibly an amniotic band may have been a factor. The relations of this condition with cryptophthalmos and congenital symblepharon are discussed.

Gifford, Chicago. [Arch. Ophth.]

Vitamin C Content of Aqueous and Crystalline Lens: Relation to Cataract. G. Bietti, Boll. d'ocul. **18**:3 (Jan.) 1935.

Bietti examined the aqueous and lenses of animals with naphthalinic cataract and of patients with various types of cataract. In the naphthalinized animals a marked reduction in cevitamic acid was found, which was in general proportionate to the degree of opacity. Of the ten patients a marked reduction of cevitamic acid in the aqueous was shown in all but one, a child with zonular cataract. The vitamin was most reduced in two patients with cataracta nigra and nuclear cataract and in aphakic eyes, less so in intumescent senile and in traumatic cataract. Reduction of the amount in lenses removed at operation was equally marked, especially in cases of sclerotic and black cataract. The amount in eyes of rabbits submitted to irradiation with the roentgen rays was also reduced. Hence the presence of cevitamic acid seems to depend not only on the presence of the lens but on its vitality. Fischer believed that cevitamic acid ($C_6H_8O_6$) is formed in the lens by dehydrogenation of a molecule of dextrose in the presence of a hydrogen acceptor (amino-acetic acid). Bietti found that by administering large amounts of orange juice to rabbits the amount of cevitamic acid in the blood was almost doubled, and likewise that in the aqueous, while that in the lens showed only a slight or no increase. In the dog, however, the amount in the aqueous remained unchanged, and that in the blood showed only a slight and very fleeting increase. Animals with experimental infection of one cornea showed a marked reduction in the cevitamic acid of the aqueous, which may indicate an interference with the permeability of the ciliary epithelium to this substance. Bietti believes that dehydrocevitamic acid, which is present in the blood stream in amounts equal to that in the aphakic eye, passes through the ciliary processes into the aqueous and that here in the presence of a normal lens it accepts hydrogen to form reduced cevitamic acid.

In discussing the possible relations of vitamin C deficiency to cataract, Bietti favors the view that deficiency of cevitamic acid in the aqueous is the result rather than the cause of cataractous changes in the lens. He was not able to prevent or influence naphthalinic cataract by administering vitamin C.

Gifford, Chicago. [Arch. Ophth.]

A CYSTICERCUS OF THE CONJUNCTIVA. F. CONTINO, Ann. di ottal. e clin. ocul. **63**:843 (Nov.) 1935.

Contino's patient was a youth of 17 years who had noticed a fleshy growth on the bulbar conjunctiva of the right eye for twenty days. The nodule was 12 by 9 mm. in size and about 6 mm. thick and was located between the insertions of the superior and internal rectus muscles. It was painless and adherent to the sclera. An exact diagnosis was not made, but when the growth was removed for diagnostic purposes it was found to contain a dense membrane, out of which escaped a transparent cyst 6 by 4 mm. in size. This was found to be a characteristic larva of Taenia solium. In from one fourth to one ninth of the cases in which a cysticercus has involved the ocular structure it has been reported as involving the conjunctiva. The diagnosis is difficult in the stage in which the cyst is surrounded by inflammatory tissue so that the parasite is invisible.

GIFFORD, Chicago. [ARCH. OPHTH.]

LEBER'S HEREDITARY ATROPHY OF THE OPTIC NERVE. HORACIO B. MOULIÉ and JUAN HURTAULT, Arch. de oftal. de Buenos Aires **10**:677 (Sept.-Oct.) 1935.

The authors refer to the symptoms and to the usual matriarchal heredity in male members, with only occasional occurrence in the females, as pointed out by Bell, and review the literature. They then present four cases of atrophy of the optic nerve in three males and one female in one family (another brother and sister had died in infancy), with the atrophy coming on at from 8 to 15 years of age, after an acute onset, and coming to a standstill with permanent reduction of vision and a central scotoma. Neither their parents nor their children showed any signs of the disease; the latter were, however, all under 14 years of age. The serologic and clinical data were irrelative. FINLAY, Havana, Cuba. [ARCH. OPHTH.]

HEMANGIOBLASTIC SARCOMA OF THE EYELID: SYSTEMATIC DIVISION OF THE ANGIOBLASTIC TUMORS. F. RINTELEN, Klin. Monatsbl. f. Augenh. **94**:463 (April) 1935.

Rintelen reports a case of hemangiosarcoma endotheliomatosum in a girl aged 14. Four months prior to her admission to the hospital nothing could be seen on the lower lid of the left eye; three months prior, a dark red wart the size of a pinhead could be seen. On admission the tumor had a base 8 mm. in diameter and a height of 1 cm. It could not be moved over its layer. Some of its cells greatly resembled those of a spindle cell sarcoma. Rintelen therefore considered it malignant.

In the second chapter of his paper Rintelen discusses the unsatisfactory classification and confusing nomenclature of these tumors. He proposes this division:

1. Homeotypical forms: (*a*) angioma simplex, (*b*) angioma cavernosum and (*c*) angioma endotheliomatosum. These are benign.

2. Heterotypical forms: (*a*) angiosarcoma simplex, (*b*) angiosarcoma cavernosum and (*c*) angiosarcoma endotheliomatosum. These are malignant.

Both types may originate (1) from lymph vessel tissue and (2) from blood vessel tissue.

Incidentally Rintelen rejects the synonym "telangiectasia" for "simple angioma," which designates a frequently congenital new formation of blood vessels; telangiectasia is an acquired enlargement of normally existing vessels. The term "naevus flammeus" should be used in ophthalmology only in reference to those nevi in which the characteristic nevus cells composing these tumors have been observed histologically.

STOLL, Cincinnati. [ARCH. OPHTH.]

Skin Diseases; Allergy

ERYTHEMA ANNULARE RHEUMATICUM. ARTHUR F. ABT, Am. J. M. Sc. **190**:824 (Dec.) 1935.

Erythema annulare rheumaticum (Lehndorff and Leiner) is a specific exanthem associated only with rheumatic endocarditis. The lesions are pale red or bluish red semicircles or rings which on first appearance may be from 2 to 4 mm. in diameter and which may develop into rings of from 1 to 3 cm. in diameter. The lesions are found on the chest, over the abdomen, on the sides of the thorax and on the back. They are rarely seen on the extremities and never on the face or mucous membranes. The lesions are never papular but always macular. No itching, edema or hemorrhage is associated with them. They disappear without scaling or pigmentation.

Lehndorff estimated that erythema annulare rheumaticum occurs in about two thirds of all cases of rheumatic endocarditis in children. Because of its transitory nature it is often overlooked. The rash is not associated with septic or ulcerative endocarditis or endocarditis lenta and does not occur in other types of arthritis. It never occurs at the onset of an attack of acute rheumatic fever and appears only following the endocardial involvement. In fact, it so constantly indicates the persistence of a rheumatic infection in association with cardiac involvement that it has been said that rheumatic endocarditis may be diagnosed by merely seeing this rash on the skin.

The exact nature of the rash is unknown. No one has as yet established a relationship between this eruption and the tuberculin reaction, or the demonstration of tubercle bacilli by gastric lavage, as has been done in erythema nodosum.

The only reported histologic examination of the skin in a case of erythema annulare rheumaticum is the one of Carol and Van Krieken.

It may be concluded that erythema annulare rheumaticum is exclusively associated with rheumatic endocarditis, and its appearance has been noted only in association with this disease. The occurrence of this rash in children who are suffering from rheumatic endocarditis, as is the case with other cutaneous lesions found in this disease, may be considered either as evidence of the persistence of an active rheumatic endocarditis or as a sign of reactivation of the disease.

HENSKE, Omaha.

PACHYONYCHIA CONGENITA: REPORT OF A CASE. A. W. SOHRWEIDE, Arch. Dermat. & Syph. **32**:370 (Sept.) 1935.

Sohrweide reports a case of pachyonychia congenita in a Jewish boy 8 years old who was admitted to the hospital because of thickening of the nails of the hands and feet and an eruption on the feet and ankles. The description of the lesions in this case corresponds to that of the lesions in other cases reported in the literature. A table comparing the several cases of pachyonychia congenita reported in the literature and several photographs of this patient's lesions are included. The results of chemical studies of the blood with special mention of arsenic, are given. The possibility that pachyonychia congenita may be an allergic manifestation is mentioned.

DULIN, Iowa City.

GANGRENE OF A NEVUS OF THE FOOT IN AN INFANT. H. HALLÉ and JACQUES LEVEUF, Bull. Soc. de pédiat. de Paris **32**:523 (Nov.) 1934.

A girl, 6 weeks old, was admitted to the Bretonneau Hospital because of a large ulcer on the dorsum of the right foot at the site of a hemangioma. The mother had noticed a small reddish area, which had begun to ulcerate, when the baby was 4 days old. The infected gangrenous area was exposed to warm air and more than two months was required before the infant was discharged from the hospital. The ulcerated area had completely cicatrized, and one could

discover hardly any evidence of angioma. Hemangioma was present on the sole of the foot which had been incised, because a fluctuating swelling was palpated, but only blood was obtained and no pus. The infant had a temperature characteristic of sepsis, and the general condition was poor. Repeated blood transfusions were given. A blood culture revealed streptococci. The explanation is offered that the skin sloughs and infection of the tissues takes place because the process of repair cannot keep pace with the rapidity of growth of the underlying hemangioma.

BENJAMIN, Montreal, Canada.

VARIOUS CASES OF ACRODYNIA AND THE TREATMENT. P. DUHEM and ERNEST HUANT, Bull. Soc. de pédiat. de Paris **32**:527 (Nov.) 1934.

Six cases of acrodynia in children, ranging in age from 1 to 14 years, are described. Cases of hypotonicity for which no definite cause can be found should suggest the possibility of acrodynia. The first improvement which generally takes place is to be observed in the tone and disposition; this occurs long before any marked amelioration of the trophic disturbances becomes evident. Investigation of the neurovegetative responses, such as the oculocardiac reflex and the cardiac acceleration, after the subcutaneous injection of a solution of epinephrine is advised, both as an aid to diagnosis and as a guide in physical therapy. It is believed that the most probable etiologic factor in this disease is neuro-endocrine.

BENJAMIN, Montreal, Canada.

THREE ADDITIONAL CASES OF INFANTILE ACRODYNIA. JULIEN LAMORIL, J. de sc. méd. de Lille **53**:245 (March 10) 1935.

The author considers infantile acrodynia to be due to infection by an unknown neurotropic filtrable virus resembling those of encephalitis and poliomyelitis and capable of reactivation by measles or any intercurrent infection having a filtrable virus and of survival in a clear medium. This hypothetic virus may cause diffuse and superficial changes in the spinal cord and the neurovegetative system, with selective preference for the centers in the infundibulotuberal region, a preference which explains the extent and diversity of the symptoms, the frequency of occurrence of the complaint, as it always appears as a sequel to an intercurrent infection, and the full restoration in most cases. The disfiguring form seems to be the exception.

VINTON, Brooklyn.

ERYTHRODERMA DESQUAMATIVUM (LEINER-MOUSSONS' DISEASE). G. BLECHMANN and P. J. MÉNARD, Nourrisson **23**:89 (March) 1935.

In the case reported enterococci were recovered from the desquamating epidermis. On the supposition that these organisms might be the etiologic factor, an autovaccine was prepared and administered in small doses by mouth. Rapid recovery took place. The treatment merits further trial.

MCCLELLAND, Cleveland.

STUDIES ON INFANTILE ACRODYNIA: I. NOTE ON THE YEARLY AND SEASONAL INCIDENCE. E. LEENHARDT and J. BOUCOMONT, Rev. franç. de pédiat. **11**:265, 1935.

In the course of the last seven years the authors have observed thirty-eight cases of acrodynia. The number has increased yearly, and in 1934 fifteen cases were seen. By far the greatest number were seen in the winter and spring months. The authors raise the question as to whether acrodynia is a neurovegetative localization of a banal infection of the respiratory passages. They also cite the hypothesis of Moro that there is hyperexcitability of the vegetative nervous system in the spring, which in certain infants may take the form of acrodynia.

LESLIE, Evanston, Ill.

STUDIES IN INFANTILE ACRODYNIA: II. CAPILLAROSCOPY. J. BOUCOMONT and R. LAFON, Rev. franç. de pédiat. **11**:272, 1935.

In ten cases of acrodynia studies were made with the capillaroscope. In all the cases abnormal dilatation of the subpapillary plexus was shown, with increase in the number of capillaries. This was more difficult to see in the later stages, when thickening of the epidermis had occurred. The rapidity of the capillary circulation was for the most part within normal limits.

LESLIE, Evanston, Ill.

SPECIFIC SEROTHERAPY IN CASES OF CUTANEOUS CARBUNCLE. G. RIGGIO, Pediatria **43**:534 (May) 1935.

Riggio presents a critical review of the literature on the various methods of the treatment of carbuncle and reports six cases in children between 10 months and 10 years of age in which he utilized serotherapy. The serum was administered subcutaneously in doses varying from 10 to 50 cc., and the injections were repeated daily for from four to six days.

His results were remarkable not only because cure was obtained in 100 per cent of the cases but especially because of the immediate response of the condition from the standpoint of the local and the general disappearance of symptoms.

SIGNORELLI, New Orleans.

ACRODYNIA INFANTUM. V. PARDO-CASTELLÓ and RAMON IBARRA PÉREZ, Arch. de med. inf. **4**:1 (Jan.-March) 1935.

The child was a Negro, 4½ years of age. The onset was characterized by paralysis and convulsions. These symptoms disappeared and were followed by the symptoms typical of erythroderma. The authors believe that this confirms the view that erythroderma represents a disease of the nervous system, with secondary trophic and circulatory manifestations of the skin and peripheral polyneuritis.

SANFORD, Chicago.

FURTHER CONTRIBUTIONS TO THE CAUSE OF IMPETIGO CONTAGIOSA ALBO-STAPHYLOGENES (DOHI). HARUKO ASANO, Jahrb. f. Kinderh. **144**:222 (April) 1935.

The point is emphasized that heretofore Japanese authors have looked on Staphylococcus albus as the sole etiologic factor in the contagious dermatosis occurring in the summer months in children from infancy to 3 years of age.

The author in the years from 1930 to 1933 undertook bacteriologic studies in one hundred and fifty-eight cases of this condition. He found that in 72.8 per cent the disease was due to Staph. albus, in 18.3 per cent, to Staphylococcus aureus and in 8.9 per cent, to Staph. aureus and Staph. albus mixed.

He was able to reproduce the condition in sixteen infants by implantation experiments with Staph. aureus isolated from patients who had previously had the disease.

From these results he concludes that Staph. aureus is also an etiologic factor, and he proposes the new name impetigo (contagiosa) staphylogenes infantum.

LANDAU, Rochester, N. Y.

CONGENITAL ICHTHYOSIS. W. COURTIN, Ztschr. f. Kinderh. **55**:384 (Sept.) 1933.

Courtin reports a case of an infant born 4 weeks prematurely, with no family history of disease of the skin, who from the first day of life showed cornification of the skin. The picture was that of erythrodermie congénitale ichthyosiforme, described by Brocq. The author could find no etiologic factor for the disease. He excluded syphilis.

LEVINSON, Chicago.

A Case of Weakness of the Connective Tissue. V. Mayr-Weber, Ztschr. f. Kinderh. **55**:472 (Sept.) 1933.

Mayr-Weber reports a case of a 6 year old boy whose skin was found to have loose connective tissue, so it could be lifted in large folds.

Levinson, Chicago.

Cases of Vegetative Neurosis (Feer's Disease). T. Varga, Orvosi hetil. **79**:379 (April 6) 1935.

Three cases are reported. The first child, aged 3 years, had severe itching of the palms and soles, so that they had to be scratched with a brush, even in the night, and the child could not sleep because of the itching. Other symptoms were also found, such as acrocyanosis, excessive perspiration, hypotonia decrease of the reflexes, etc. The second child, aged 4 years, had the same symptoms, but the itching was not so severe as in the first case. The third case was that of a 10 year old girl. The illness began with fever, which lasted one week. The typical symptoms of Feer's disease were also to be found, but the mental depression and the disorders of motion and sleep pointed to encephalitis. It seems that there are borderline cases, in which the condition forms a transition between Freer's disease and encephalitis.

Göttche, Budapest, Hungary.

A Case of Ecthyma Gangraenosum Cachecticorum Producing a Destructive Ulceration of the Cranial Bones. T. Akima, Jap. J. Dermat. & Urol. **37**:470 (April) 1935.

A 3 month old girl had fever and an exanthem; later erythematous areas appeared, and subcutaneous infiltration, suppuration and, finally, ulceration developed. The ulcers in the right temporal region became confluent, forming a single huge ulcer half the size of the palm and finally exposing a section of the skull. At he same time lesions like ulcers with sharply cut, steep borders developed on the sacral and the occipital region, on the lips and on the labium majus. A section of bone was finally extruded from the temporal region, and the ulcers, including that of the temporal region, eventually healed, leaving much scarring.

Cases such as this, in which the lesion not only involves the subcutaneous and muscular tissues but actually reaches down and involves the bone, are extremely rare and have not been observed before in Japan.

From the pus of the disease foci Bacillus pyocyaneus and Staphylococcus aureus were isolated on agar culture mediums.

J. W. Brennan, Chicago. [Arch. Dermat. & Syph.]

Microscopic Pathologic Features of the Erythema Annulare of Lehndorff and Leiner. W. L. L. Carol and J. A. van Krieken, Acta pædiat. **17**:372, 1935.

This brief paper contains a description of the histologic features of a specimen of tissue removed from a patient with rheumatic erythema annulare; four photomicrographs are reproduced. The microscopic characteristics are those associated with acute inflammation of the upper and middle layers of the cutis, and they differ from those observed in cases of erythema exsudativum multiforme (Hebra) and of urticaria annularis.

McCune, New York.

Treatment of Erythema Nodosum (Erythema Induratum Bazain) with Injections of the Patient's Own Blood. Johannes Heimbeck, Norsk mag. f. lægevidensk. **96**:390, 1935.

Two patients suffering from erythema nodosum chronicum with ulcerations were treated with intramuscular injections of autoblood given in small weekly doses—1, 1.5 and 3 cc. and later 3 cc. during from two to three months. The ulcerations healed, and the erythema disappeared.

Toverud, Oslo, Norway.

Case of Erythema Annulare (Lehndorff and Leiner). J. A. van Krieken, Maandschr. v. kindergeneesk. **4**:224 (March) 1935.

A description is given of a case of the erythema annulare of Lehndorff and Leiner in a girl, aged 7 years, who was admitted to the hospital for the treatment of gonorrheal vulvovaginitis. During her stay in the hospital acute rheumatic fever developed, with rheumatic endocarditis and annular erythema.

van Creveld, Amsterdam, Netherlands.

Surgery and Orthopedics

Some Distressing Consequences of Circumcision During the Diaper Wearing Period. Frank van der Bogert, Arch. Pediat. **52**:562 (Aug.) 1935.

The common practice of routine circumcision of new-born infants is deplored. In the author's opinion, retraction of the foreskin and breaking up of adhesions will in most instances accomplish the desired results. This procedure does not have associated with it certain changes following circumcision. It is suggested that overconfidence in surgical technic and an overzealous attitude toward preventive medicine encourages an unwarranted disregard of the functions of an organ provided by nature for a definite purpose. Attention is called to certain conditions which may result from or are aggravated by circumcision.

Waddell Jr., University, Va.

Physiological Postural Deformities in Contrast to Pathological Postural Deformities. Carl E. Badgley, J. Michigan M. Soc. **34**:469 (Aug.) 1935.

Badgley accepts the belief that there are physiologic deformities which disappear through the process of growth and development but queries, "Are we well enough acquainted with these normal deformities to distinguish them from pathological deformities?" In his experience, the framework of the child gets little or no attention from the parent or the physician once the child begins to dress itself. Rarely is a child referred to the physician for postural study. The author pleads for a competent examination of young school children; from 10 to 26 per cent may show varying degrees of scoliosis. Eighty-five per cent of the freshmen class of both Harvard University and Yale University showed deformities; many of these were mild, but others were sufficiently severe to unfit students for service in the army. Among the physiologic deformities which may be corrected by time are bowlegs, early genu valgum, lordosis and pendulous abdomen. All these conditions appear in early childhood and are frequently cured by the process of development. Postural defects which are present in children from 4 to 5 years of age apparently do not disappear but rather grow more severe unless treatment is instituted. By 12 years of age the patient with scoliosis generally has a well marked structural deformity of the spine, for the treatment of which present day methods are not entirely successful. Badgley reiterates his oft-expressed opinion that "our hope is without the prescoliotic and in devising methods of preventing his going on to scoliosis."

Carey, Detroit.

Early Spondylolistheses; Case Report. Ralph M. Carter, Wisconsin M. J. **34**:552 (Aug.) 1935.

A girl not quite 9 years old is the youngest patient with spondylolisthesis reported on, with the exception of an infant in whom the condition was congenital.

The development seemed to be spontaneous, and there were no symptoms except the difficulties arising from mechanical causes. In this child, who had previously been well, the following disorders had rapidly developed for eight weeks:

deformity of the lumbosacral region, with scoliosis, and shortening and depression of the lumbar part of the spine, there being a complete forward dislocation of the entire upper part of the spine on the sacrum.

A posterior bone graft from the tibia was inserted for stabilization. When the patient was last seen there was no change in the deformity.

JANNEY, Wauwatosa, Wis.

POSTOPERATIVE ANURIA IN A CASE OF "RENAL FRAGILITY." DOUBLE DECAPSULATION. CURE. JACQUES LEVEUF and HENRI GODARD, Bull. Soc. de pédiat. de Paris **33**: 35 (Jan.) 1935.

A girl, 10 years old, had an appendectomy, under general ether anesthesia. Her urine before operation was normal. Four days later she complained of severe abdominal pain and vomited repeatedly, although she had a stool. She passed a few ounces of urine in the morning, but thereafter there was complete anuria, and she became blind. Examination of the blood urea showed marked retention. Medication with intravenous injections of saline solution, as well as with diuretics, brought about no improvement. Renal decapsulation was performed the following day. Both kidneys were about twice the normal size; they bulged through the incisions in the capsules and were friable, one having torn slightly near its hilus. Fragments of each kidney were removed for biopsy, and histologic examination of these showed marked changes. There was postoperative diuresis, and the blood urea content began to return to normal soon after operation. There was a slightly diminished output of phenolsulfonphthalein. Whether the release of intracapsular renal pressure or the section of sympathetic nerve fibers was responsible for the diuresis cannot be answered definitely. How much the ether or the toxic absorption due to operative trauma associated with appendectomy may have had to do with the abnormal sequelae is not known, but it is considered that the child had so-called renal fragility, a condition of impaired renal resistance, as a result of heredity and possible previous renal injury, and that as a consequence the kidneys were unable to take on the extra load occasioned by the operation. It is in such cases rather than in cases of definite nephritis that bilateral renal decapsulation is indicated, and a good result may be expected if surgical intervention is not delayed too long.

BENJAMIN, Montreal, Canada.

THE MOST FREQUENT ACCIDENTS AND COMPLICATIONS OF EXTRAMUCOSAL PYLOROTOMY (THE FREDET-RAMMSTEDT OPERATION). AUGUSTÍN CASTELLANOS, Bol. Soc. cubana de pediat. **6**:355 (Nov.-Dec.) 1934.

Castellanos reports several illustrative cases and enumerates some of the accidents and complications of extramucosal pylorotomy. Among these he mentions injury to the mucosa during operation; generalized peritonitis; hemorrhage in the incision and in the abdominal wall; separation of the abdominal sutures; hepatic insufficiency, with acidosis; hypochloremia, with alkalosis; postoperative pneumonia, the persistence of the vomiting, owing to insufficient section of the obstructing, constricting fibers of connective tissue.

SCHLUTZ, Chicago.

SPORTS AND TRAUMA DUE TO SPORTS. OCTAVIO C. FERNANDEZ, Med. de los niños **36**: 198 (July) 1935.

This article discusses the more common injuries occurring in sports. The majority of such injuries result from the fact that the player is not prepared to protect himself. The author stresses the importance of kinestherapy in this type of injury. Among the most common traumas are luxations of the shoulder joint. These traumas are improved by massage to relax the muscles, then by reduction, followed by immobilization. Later, more massage and passive movements under skilled guidance are helpful.

The treatment of fractures, muscle tears, tendovaginitis and bursitis is discussed in some detail.

TREATMENT OF BURNS WITH A PARAFFIN DRESSING. E. BALTODANO BRICEÑO, Med. de los niños **36**:300 (Oct.) 1935.

A paraffin dressing is preferred to all other medicaments in the local treatment of burns. This product does not adhere to the surfaces; pain is diminished, and scar formation is minimized. After the burned area is cleaned, paraffin may be applied on gauze. Supportive therapy is also important, and among such measures are transfusion, hypodermoclysis of saline solution, injections of epinephrine hydrochloride and the administration of cardiac stimulants. The author believes that the use of morphine to combat shock is contraindicated.

DWYER, Kansas City, Mo.

BODY POSTURE IN SICK CHILDREN. MARJA STOBIECKA, Pedjatrja polska **15**: 75, 1935.

After a somewhat extensive study the author came to the following conclusions:

1. Children from poor homes have a poor body posture.
2. Children from centers where tuberculosis exists, are subject to poor posture.
3. Sickly children have poor posture.
4. Poor posture is found more often in children with bad teeth, enlarged lymph glands and tuberculous infections than in normal children.
5. Poor posture is often only temporary and is usually due to a weakened condition of the child, caused by disease.

KRUPINSKI, Chicago.

PERINEAL HERNIA; REPORT OF CASE. TAI WAI WONG, Chinese M. J. **49**:760 (Aug.) 1935.

Perineal hernia, which is a rare abnormality, was seen in a girl, aged 6 weeks, at the Leung Kwong Baptist Hospital in Canton. The swelling was located between the anus and coccyx and was present at birth. Care was taken in the diagnosis to rule out spina bifida occulta as the cause of the sac. The parents were warned of the hazard of surgical intervention, but they insisted on operation. When the skin and serous lining of the sac were opened, an entrance into the peritoneal cavity was seen, with protrusion of a short loop of colon. The sac was removed, but the child died of shock within a few hours.

The author believes that the diagnosis of perineal hernia is correct, though a sacrococcygeal teratoma might be in question. The lining of the sac, however, was peritoneum, and the presence of the intestine in the neck of the sac indicates a true hernia.

NEFF, Kansas City, Mo.

Miscellaneous

INTRAVENOUS TOXICITY OF ATABRINE (ATEBRIN). W. T. DAWSON, WENDELL GINGRICH and E. D. HOLLAR, Am. J. Trop. Med. **15**:515 (Sept.) 1935.

The authors review briefly the literature on the toxicity of atabrine and report their experience with this drug. They experimented with rabbits, and their conclusions are based on the results of some two hundred and fifty intravenous injections.

They concluded that, owing to the slow excretion or destruction of atabrine in the body, it seemed unnecessary to exceed for intravenous injection the dose of 0.1 Gm. for the adult. The margin of safety is probably not great, and intravenous injections should be made only in emergencies. The injection should be made slowly and timed to take several minutes for completion. The total amount of the drug injected over a period of twenty-four hours should not exceed 0.3 Gm., and a course of treatment should not be repeated within eight weeks. The drug should always be taken under the supervision of a physician.

BURPEE, Augusta, Ga.

A Consideration of Genetic and Developmental Factors from the Pediatric Viewpoint. Gaylord W. Graves, Arch. Pediat. **52**:649 (Oct.) 1935.

The principles of inheritance are discussed in detail. Because of the potentialities latent in the respective parental cells destined to undergo cell union, as well as the wide range of modifying conditions, both nutritional and mechanical, to which the undeveloped organism is subjected, it is necessary that the clinician keep in mind certain fundamental principles of heredity and embryology. Such knowledge should make for greater accuracy in diagnosis and prognosis. By way of illustration four case histories are briefly presented.

Waddell Jr., University, Va.

The Effect of Ephedrine on the Emptying Time of the Human Stomach. E. J. Van Liere, D. H. Lough and C. K. Sleeth, J. A. M. A. **106**:535 (Feb. 15) 1936.

The authors found that therapeutic doses of ephedrine sulfate prolonged the emptying time of the stomach in six healthy young males. The average prolongation was 91.66 per cent. Because of the widespread use of the drug these results should be of clinical interest.

Bonar, Salt Lake City.

Twenty-Five Years of Eugenic Sterilization. Norman Fenton and Paul Popenoe, J. Juvenile Research **19**:201 (Oct.) 1935.

Fenton and Popenoe suggest that the survey in California based on over 10,000 cases will furnish valuable material on which to base further plans in the attempt to control conception among the unfit.

Hamill, Chicago.

A New Type of Castor Oil in Infancy and Childhood. B. W. Jarvis, M. Rec. **142**:513 (Dec. 4) 1935.

In the summary and conclusion the author states:

"An attempt was made to compare the action of a highly refined castor oil with that of ordinary castor oil found in stores.

"Ordinary oil was given eleven patients, of whom nine vomited and six had cramps or colic.

"Highly refined oil was given forty-six patients, of whom three vomited and two had colic.

"An important advantage of the highly refined oil was the absence of taste and the ease with which it is taken, even to those who had previously been unable to take castor oil.

"Untoward effects from common castor oil is probably due to rancidity and impurities."

Williamson, New Orleans.

The Black Widow Spider. William H. Allen, Mil. Surgeon **77**:352 (Dec.) 1935.

Death may result in a small child from the bite of the black widow spider, and the symptoms are sufficiently severe to warrant prompt and effective treatment. If the bite can be found, small incisions should be made over it and the wound drained by suction. For the agonizing pain 10 cc. of a 10 per cent solution of calcium gluconate may be given intramuscularly. This injection may be repeated as needed (Gilbert and Stewart have given it intravenously). Additional measures include hot packs, baths, and catharsis to hasten elimination.

Sanford, Chicago.

Disease of Childhood from the Standpoint of a General Practitioner. A. E. Buchanan, Nebraska M. J. **20**:382 (Oct.) 1935.

Buchanan stresses the importance of heredity in diseases of children and emphasizes the necessity for better care of children on the part of the practitioner.

Hamilton, Omaha.

ILLEGITIMACY. J. FREIRE DE VASCONCELOS and JOSÉ SAMPAIO, Arch. de pediat., Rio de Janeiro **7**:39 (Nov.) 1935.

This excellent article deals with the increase in illegitimacy and the high mortality among illegitimate infants. In brief, there is an increase in the number of illegitimate births in all countries. The authors present tables. In the United States in 1876 there were 9 illegitimate births per hundred births, and in 1913, 9.7. Of even more interest is the higher death rate among illegitimate than among legitimate infants. The data are also given in tables for various countries. For example, in England the mortality rate is 14 per cent for legitimate, and 35 per cent for illegitimate, infants. Persons interested in this problem will find the article of interest. [Unfortunately, social service workers, who contribute to this mortality by separation of illegitimate infants from their mothers at birth, will not read this—H. S.]

SANFORD, Chicago.

TRANSFUSION IN PEDIATRIC PRACTICE. CARLOS URRUTIA U., Rev. chilena de pediat. **6**:459 (Oct.) 1935.

Transfusion is a useful and indispensable procedure in pediatric practice. In the infant the longitudinal sinus or the external jugular vein is the vessel of choice; in the older child, the jugular vein or the vessels of the arm.

For the infant the author advises indirect transfusion with fresh citrated blood. He does not advise the use of blood which has been kept for some time or blood taken from a cadaver. In the very young infant, small amounts must be used—about 15 cc. per kilogram of body weight. It must be given slowly, at the rate of about 5 cc. a minute. As a preoperative measure to combat shock, the author recommends two transfusions given about one week before the operation. More can be given if a major procedure is contemplated. Females are to be preferred as donors.

In Chile group IV is the most common blood group. SCHLUTZ, Chicago.

LEAD POISONING IN INFANTS AND YOUNG CHILDREN. M. KASAHARA and S. NOSU, Ztschr. f. Kinderh. **55**:577, 1933.

According to Kasahara and Nosu, lead poisoning in infants and young children is frequently observed in Japan. It is due to the intake of breast milk containing lead, the lead being transmitted to the milk by lead-containing powder and other cosmetics used by the nursing mother over a long period. The mother, however, does not show any symptoms of lead poisoning. The authors found amounts of lead varying from a trace to 0.8 mg. per liter in the mother's milk in cases of lead poisoning in infants. The severity of the clinical manifestations in lead poisoning of infants is not necessarily dependent on the amount of lead in the milk. The lead may continue to be present in the mother's milk even after the mother has discontinued the use of lead-containing articles. The authors have proved the transmission of lead to milk by subcutaneous injection of lead salts into goats. They have also found that the lead content of the milk in the experimental goats is higher than the lead content of the blood and that when the lead is transmitted to the milk through the skin the amount is not as great as when it is injected subcutaneously.

LEVINSON, Chicago.

LEAD POISONING IN INFANTS AND CHILDREN. M. KASAHARA and M. NAGAHAMA, Ztschr. f. Kinderh. **55**:583, 1933.

Anemia due to lead poisoning in Japanese breast-fed infants is described by Kasahara and Nagahama. The authors believe that this should be considered as a distinct type of anemia.

LEVINSON, Chicago.

Society Transactions

AMERICAN PEDIATRIC SOCIETY AND CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

Joint Meeting, Bolton Landing, Lake George, N. Y., June 11-13, 1935

FRITZ B. TALBOT, M.D., *President, in the Chair*

Fourth Session

Friday Evening, June 12

(Concluded from page 1039)

A CASE OF DIABETES MELLITUS REFRACTORY TO INSULIN THERAPY. DR. HOWARD H. MASON (by invitation), New York.

A white boy, aged 2 years, was admitted to the Babies Hospital because of glycosuria, which had been discovered when he was 18 months old. The sugar in the urine was identified as dextrose. The blood sugar during fasting was never high. After a mixed meal the value for the blood sugar rose promptly to between 200 and 400 mg. per hundred cubic centimeters, then fell gradually until the next feeding. When the patient was on a mixed diet containing 90 Gm. of carbohydrate, the twenty-four hour specimen of urine contained from 30 to 50 Gm. of dextrose. Insulin did not keep the blood sugar content within normal limits or stop the glycosuria.

Elimination from the diet of all carbohydrate, which is changed to dextrose in digestion, resulted in an approximately normal blood sugar level and the excretion of little or no dextrose in the urine.

The response to epinephrine was normal. The response to insulin was abnormal. If insulin was given when the patient was fasting and the blood sugar content was low there was no prompt drop in the blood sugar content, but a gradual rise and a steady fall. Even 100 units of insulin given intravenously shortly after the ingestion of a mixed meal had no apparent effect on the height of the blood sugar level, which continued to rise steadily.

Some carbohydrate was being burned, for the excretion never equaled the intake. Furthermore, the respiratory quotient during fasting averaged 0.78. After a mixed meal or 90 Gm. of dextrose in divided doses was given it rose to 0.85. After 90 Gm. of sucrose in divided doses was given it rose to 0.91.

From these facts it appeared that this was not an ordinary case of pancreatic diabetes. It seemed as though the patient used what dextrose he could but was unable to store the excess for future use, so he excreted it. If this was true, he should be able to ingest some dextrose without showing glycosuria, provided the dextrose was given in sufficiently small amounts to prevent raising the blood sugar content above the renal threshold and the intervals between feedings were long enough to allow him to metabolize most of the dextrose taken at one feeding before he received the next. With this in mind my associates and I gave him 240 cc. of milk every four hours for five feedings a day. On this regimen he excreted about 3.6 Gm. of dextrose in twenty-four hours. His blood sugar content reached 207 mg. per hundred cubic centimeters at 5 p. m. The other determinations were below 146 mg. per hundred cubic centimeters.

If the difficulty of storage is confined to dextrose he should be able to take some added levulose. Ten grams added to each feeding of milk increased the excreted sugar by only 1 Gm.

The evidence suggests that the glycosuria was due not to an insufficient amount of insulin or to a lowered renal threshold but to a lowering or absence of ability, probably on the part of the liver, to change dextrose into glycogen. There would seem to be no lessening of the liver's ability to convert the other precursors to glycogen. This hypothesis would explain why insulin had so slight an effect and would make the condition dependent on defective liver function, as are galactosuria and levulosuria.

INFANTS OF DIABETIC MOTHERS. DR. WARREN R. SISSON and DR. PRISCILLA WHITE (by invitation), Boston.

Diabetes is recognized as a hazard to the successful termination of pregnancy. Statistics show that between 40 and 60 per cent of infants of diabetic mothers die either during gestation or in the neonatal period. The common causes of death have been trauma sustained at birth, due to oversize of the infant, maceration and prematurity.

The use of insulin in the treatment of diabetes has greatly increased the number of diabetic mothers of child-bearing age. The incidence of pregnancy of diabetic mothers has also increased. The mortality of the group of infants of diabetic mothers has not been notably reduced in the era of insulin.

The present study was made on 27 infants of 25 diabetic mothers. These were consecutive patients in the clinic for patients with diabetes of Dr. Elliott P. Joslin at the New England Deaconess Hospital in Boston. The diabetes was in some instances, mild, controlled and of short duration; in others it was severe and often uncontrolled by insulin. In many instances the disease started in early childhood. It is this group of babies with so-called "juvenile diabetes" that increases the number of infants of diabetic mothers. Sixteen babies in this series were delivered by cesarean section.

The following observations were made: The weights of these infants were slightly above the normal standards. No "giant" babies were present in this series. This may be explained in part by the fact that some of the infants were delivered before term by cesarean section. One can definitely conclude that none of these babies that survived was larger skeletally than a normal infant.

The blood sugar values for these infants at birth and at intervals after birth showed no deviation from the normal with one exception: One infant had a blood sugar content of 9 mg. per hundred cubic centimeters eight hours after birth and symptoms of hypoglycemia, which were undoubtedly caused by the administration of insulin to the mother just prior to delivery.

The following signs and symptoms were noted: Edema, similar to that known as edema of the new-born, was frequently seen. Cyanosis was a common sign. This occurred usually from three to four hours after birth. It was similar to the cyanosis in asphyxia of the new-born. Convulsions occurred in 1 instance.

Autopsies showed evidences of prematurity, atelectasis and cerebral hemorrhage. The islands of Langerhans were considered hyperplastic in 2 instances.

No definite correlations between the type of diabetes and the condition of the infant could be made. Normal infants were born of diabetic mothers after coma.

There were eight fatalities in this series, or a mortality of 29.6 per cent. If the baby that died in the sixth month of gestation whose mother had pneumonia is excluded, the corrected mortality is 26.9 per cent.

PROTAMINE INSULIN IN CHILDREN. DR. GLADYS L. BOYD, Toronto, Canada.

The results of the treatment of 25 diabetic children with protamine insulin are reported. It is felt that this type of insulin offers a new hope to many patients with an unstable blood sugar content and to those who require large doses of insulin with multiple daily hypodermic injections. The reactions are fewer

and in the case of the child occur at more convenient times than those following the administration of ordinary insulin. There is a wider margin of safety both in the food allowance and in the dosage of insulin. In many cases the condition can be well controlled with one large dose daily. Its use is contraindicated when quick action is desired.

DISCUSSION OF PAPERS READ BY DR. MASON, DR. SISSON AND DR. BOYD

DR. ALLAN M. BUTLER, Boston: First, I should like to comment on the nice way in which Dr. Mason has made use of the abnormal condition in the patient to study normal physiology.

I should like to ask Dr. Mason whether he could say something about the data on his chart concerning the ketosis, which I, at least, was unable to appraise, since the presentation of the charts had to be so hurried. Then I should like to ask him whether he would care to make any comment concerning the low storage of dextrose and glycogen in his patient, the low blood sugar content and the ketosis—signs that are sometimes associated with the appearance of cyclic vomiting. His patient gave no history of such a disturbance. Third, I wonder whether he could give any idea as to the possible relation of so-called pituitary diabetes to the observations made on the patient he has studied.

Concerning the use of protamine insulin, I should like to confirm its successful use by Dr. Boyd by the gratifying results at the Children's Hospital, Boston. On the basis of our experience my associates and I see no need for hesitancy in using protamine insulin. We think that one can avoid an insulin reaction by careful observation of the sugar content of the urine and the symptoms in the patient and see no reason why one should be apprehensive in the absence of facilities for determining numerous blood sugar levels.

We think that the use of protamine insulin is ideal for the handling of the diabetic patient who has to undergo an operation.

Dr. Boyd mentioned giving protamine insulin to patients a considerable time before breakfast. My associates and I have found that if we use protamine insulin in such amounts as to allow giving a single injection per day of combined protamine insulin and old insulin before breakfast the blood sugar content before breakfast is low enough so that if added insulin is given an hour previous to the ingestion of breakfast the child is likely to have symptoms of an insulin reaction before breakfast. Therefore we have changed our practice from one of giving insulin an hour to an hour and one-half previous to breakfast to one of giving the insulin immediately before breakfast.

DR. BENJAMIN KRAMER, Brooklyn: I think that one can agree with Dr. Mason that the condition in his patient is not true diabetes. If the ability to respond with a definite rise in the respiratory quotient following the administration of dextrose can be considered as the criterion, this patient does not have true diabetes mellitus.

However, the patient undoubtedly has a severe disturbance in the handling of certain carbohydrates.

As one looks at the charts one notes that the initial blood sugar level seems to be constantly low. Second, there is a tremendous rise in the blood sugar content following the administration of various carbohydrates. There is also definite ketonuria. The wide fluctuation of the blood sugar level in a patient who can burn sugar suggests some disturbance in glycogenesis or glycogenolysis or both or in the conversion of carbohydrate into fat. The transient ketonuria indicates that at times dextrose is being oxidized in insufficient amount to permit complete combustion of fat. These observations suggest two clinical syndromes which have been recently reported. One is the syndrome of von Gierke, in which there is enlargement of the liver with ketonuria, sometimes glycosuria and at other times hypoglycemia, in which the ability to store glycogen is preserved but glycogenolysis takes place very slowly during life and even post mortem.

The other syndrome which presents a somewhat similar clinical picture is a disturbance during life of both glycogenesis and glycogenolysis, but post mortem extensive infiltration of the liver by fat is the outstanding observation.

DR. RUSTIN MCINTOSH, New York: I should like to comment on the patient whom Dr. Mason has studied because it seems to me that he bids fair to share to some extent the destiny of Alexis St. Martin of happy memory, who had an anatomic lesion of the stomach which enabled Dr. Beaumont to make physiologic studies of lasting importance. This patient has a physiologic abnormality, none the less striking because it is physiologic, not anatomic, so far as my associates and I have been able to determine, which has permitted Dr. Mason to make important studies in regard to intermediary metabolism. I think that the interpretations of his work are far reaching. Investigators have been accustomed to make studies of the physiologic processes of experimental animals and to reason by analogy that similar processes take place in man.

There is, however, great danger in reasoning in this way. For instance, some have studied certain physiologic features in the dog, but the dog does not sweat. Other workers have studied physiologic processes in the rabbit; the rabbit does not vomit. Those who have studied anaphylaxis know how singularly the guinea-pig responds to the injection of foreign protein, as compared to man.

These facts make it seem important that one carry out one's studies, so far as possible, on man, and it is only when a patient appears with a peculiarity of this kind that one can devise investigative experiments which will enable one to penetrate beyond the results that can be obtained from the study of normal persons.

Owing to this great risk, of which I have spoken, in translating results from experiments on animals to application to man and in spite of the difficulties that still exist in the interpretation of Dr. Mason's findings, it seems safer, in my opinion, to apply these results to the interpretation of normal physiologic processes in man than to make similar studies on animals and apply the results to man. This holds true whether one eventually determines that the abnormality which Dr. Mason has described resides in some component of the endocrine system or whether one attributes it to a disturbance of function of the liver.

Dr. Mason's conclusion, that this patient presents evidence of inability to form glycogen from dextrose, has been attacked in our clinic with all the skepticism that my associates and I have been able to apply to it, but so far we have not been able to penetrate the phalanx of his logic.

DR. HOWARD H. MASON, New York: In answer to Dr. Butler's question regarding ketosis, the child had acetone and di-acetic acid in the urine a great deal of the time. I did not discuss that point because of lack of time. My associates and I learned early that the excretion of ketones decreased markedly when the child received considerable amounts of any food that contained galactose or levulose. The administration of dextrose, even in large amounts, would not diminish the excretion. On the day that he received 90 Gm. of dextrose the urine showed a strongly positive reaction to ferric chloride all day.

We tried to determine his threshold for the excretion of ketones by correlating the ketogenic-antiketogenic ratio of his diet minus the sugar excreted, according to Woodyatt's formula, with the appearance of acetone and di-acetic acid in the urine. The urine showed a positive reaction to ferric chloride when the fatty acid over dextrose equaled 1 over 1 and a positive reaction to nitroprusside when the fatty acid over dextrose was 7 over 10. These are different ratios from those obtained for normal persons. Furthermore, on the original diet, which contained about 90 Gm. of carbohydrate, 45 Gm. of protein and 50 Gm. of fat, he secreted anywhere from 500 to 600 or 700 cc. of tenth-normal acid a day. On a milk diet alone or a milk diet plus a little levulose the secretion dropped to less than 200 cc. a day. In other words, it seemed to us that when he had a fair store of glycogen in the liver he burned fat much more completely or else he burned less fat.

In regard to the rôle of the pituitary, we have wondered about that and tried to answer it, but I do not feel that we have answered it one way or the other. There are some things about the child that suggest pituitary dyscrasia.

In regard to Dr. Kramer's statement, the condition does not seem to correspond to von Gierke's disease; the patient has not a particularly large liver.

He has the low blood sugar content of a fasting person. I think that it is evident that he can store both levulose and galactose but not dextrose. Furthermore, the response to epinephrine is normal.

Dr. Gladys L. Boyd, Toronto, Canada: In reply to Dr. Butler relative to the low blood sugar content that the diabetic children who are given protamine insulin have in the morning, my associates and I, too, have considerable trouble with hypoglycemic reactions in the morning before breakfast or vomiting at breakfast due to a reaction, but none the less in the same children glycosuria not infrequently occurs at from 10 to 12 a. m. True, one can overcome this by giving insulin hydrochloride immediately before breakfast. We have tried both methods, and because of the fact that we often have patients with mothers with not too much intelligence who must administer the insulin we have tried keeping the patients on one type of insulin rather than using both types. When using two doses of protamine insulin, we found that we had better control of morning glycosuria, even if there was an early reaction, by giving it longer before breakfast.

As far as its preoperative use is concerned, we have been accustomed, for simple operations such as tonsillectomy, to giving the child one third of his daily carbohydrate ration with 2 units more than a third of his dosage of insulin for the day. The patient has gone through to his evening meal and was given more carbohydrate with the evening dosage of insulin. With that procedure the patient has little or no glycosuria as a result of the operation.

In three consecutive tonsillectomies in the last few months my associates and I have left the patients on the protamine insulin only to find that they had a large amount of sugar in the urine the next day and for several days subsequently, which necessitated raising the dose of insulin in order to overcome the glycosuria in the end.

Use of Cortin (Adrenal Cortex Extract) in Experimental Chronic Fatigue. Dr. Max Seham and Robert Harris, B.S. (by invitation), Minneapolis.

The purpose of the experiments reported was twofold: (1) to approximate in rats a state analogous to chronic fatigue in man and (2) to study the effect of adrenal cortex extract on chronic fatigue in rats.

1. To produce chronic fatigue in rats we devised the following apparatus: Ten ordinary voluntary activity cages consisting of revolving circular metal and wire mesh cages 9½ inches (24.1 cm.) in diameter and 8½ inches (21.6 cm.) wide were reconstructed by welding a small bicycle sprocket to the end of the axle shaft of each cage. The cages were mounted in two rows of five, one row above the other, the whole being supported on a framework of wood and steel sufficiently rigid and accurately made so that the alinement of the sprockets might be true. On a small table below the cages were mounted a motor and appropriate gear-reducing mechanism, to which was bolted a large bicycle sprocket. A chain connected this sprocket with the ten smaller sprockets on the cages. The speed of the cages could be varied by manipulation and rearrangement of the gear-reducing devices.

Procedure.—In each experiment, the animals were first run in the unmodified activity cages to determine their normal levels of activity. A period of fifteen days was allowed for the animals to become adjusted to the revolving cages—to "hit their stride." Then, by means of Veeder counters attached to each cage records of the number of revolutions per day were obtained for periods of five or ten days. On the basis of these records 20 animals were divided into two matched groups, half being run in the forced activity cages and the other half in the unmodified cages as controls. The experimental animals were forced to move constantly for a period of several days, the cages being stopped only for two daily feedings and for weighing the animals. A qualitatively adequate diet of greater quantity than any animal consumed was provided. It consisted of one

part of a prepared chicken mash to one part of water, supplemented by cod liver oil. Since both sex and age are correlated with voluntary activity, these variables were controlled experimentally. After the experimental period the experimental animals were replaced in the voluntary cages and their activity compared with that of their controls.

Five rats were given six days of forced activity, 3,000 revolutions per day. A second group of 5 rats were given nineteen days of forced activity, 5,400 revolutions per day. The former showed a decrement of 89 per cent in voluntary activity, the latter, a decrement of 93 per cent. The former recovered completely the preexperimental level of voluntary activity in two days; the latter, in four days.

2. To determine the effect of adrenal cortex extract on voluntary activity, 5 rats were given 0.25 cc. of the extract daily for fourteen days, and 5 other rats were given 0.5 cc. Equal amounts of physiologic solution of sodium chloride were injected into the control animals. A comparison of the records for the group treated with 0.25 cc. of adrenal cortex extract and the controls shows that there was a drop in voluntary activity in both after the period of forced activity. However, the drop in the case of the animals treated with adrenal cortex extract (to 27 per cent of the normal preexperimental level) was less than in the control animals (to 11 per cent of the normal level). Furthermore, examination of the individual records shows that none of the untreated controls was as active as the most inactive animal treated with adrenal cortex extract on the first day of the period of recovery. For the second day the average for the group is still in favor of the animals treated with adrenal cortex extract, but there is some overlapping between the groups. For the third day, and for the rest of the period of recovery the differences between the groups are small, and overlapping is the rule. Such differences as are found here are probably not significant in view of the overlapping and the normal range of variability in activity in small groups of animals. The results with the series receiving 0.5 cc. of adrenal cortex extract are substantially the same as those of the other group. On the first day of the period of recovery all the animals treated with adrenal cortex extract were more active than the untreated controls. A similar trend was evident in the rest of the period of recovery. Throughout, the averages for the group favor the experimental animals, but again these differences are not significant in view of the overlapping between the groups.

DISCUSSION

DR. FRITZ B. TALBOT, Boston: Dr. McIntosh emphasized the fact that everything that happens in animals need not of necessity happen in man; however, I have been using adrenal cortex extract for a special purpose in cases of a condition which is characterized by fatigue in man, and I can say after eighteen months of use, that such fatigue, in small children, particularly, is diminished by the use of adrenal cortex extract.

I am surprised at the size of the dose that Dr. Seham found it necessary to use, because a dose of 2 cc. for an 8 year old child seemed to me to be effective. The unit of weight dose in the rat must have been several thousand times greater than this dose in the child.

The question arises whether an overdose of adrenal cortex extract can be given. So far as I have been able to determine in a relatively small group of children, the symptom of what I think is an overdose is great excitability, which does not last more than half a day, and great activity.

I am also under the impression, and here again I have not a very definite control, that one dose of adrenal cortex extract is active to some extent for at least three days. I also have the impression that supplementing adrenal cortex extract with adrenal cortex given by mouth bolsters up the effectiveness of adrenal cortex extract and makes it last much longer, so that it is not necessary in this type of child to use the preparation more than twice a week to eliminate the fatigue, which my associates and I are trying to do for a specific purpose.

DR. MAX SEHAM, Minneapolis: In regard to the dosage, it is true that we gave a tremendous dose, but since we obtained no satisfactory positive effect from the smaller doses we felt justified in trying this larger dose, which evidently gave positive results.

I think that one should be careful about using adrenal cortex extract as a routine. Grollman warned against the toxic effect from the earlier products. He said that the epinephrine and histamine that have been found in some of the preparations of adrenal cortex products have probably been responsible for some of the physiologic effects.

CLINICAL AND EXPERIMENTAL STUDIES OF THE INNERVATION OF THE HUMAN BLADDER. DR. DOUGLAS N. BUCHANAN (by invitation), Chicago.

The present knowledge of the innervation of the human bladder is reviewed. Evidence is presented in support of the contention that the automatic emptying of the bladder in cases of cord bladder is a neurogenic process rather than a mechanical one.

The effect of section of the presacral nerve in a case of long-standing overflow incontinence is described.

Observations made during operation revealed that stimulation of the peripheral end of the cut presacral nerve causes: (*a*) contraction of some "sphincteric" structure, probably smooth muscle of the prostatic urethra and prostate at the junction of the prostatic and membranous portions of the urethra and which may be termed the "sympathetic external sphincter;" (*b*) diminution in the size of the verumontanum, possibly as a result of vasoconstriction, and (*c*) emission of prostatic and seminal fluid.

UNDESCENDED TESTES: DETERMINATION OF THE GONADOTROPIC PRINCIPLE IN THE URINE AS AN AID IN PROGNOSIS AND TREATMENT. DR. JULIUS H. HESS, DR. RALPH H. KUNSTADTER (by invitation) and DR. WILLIAM SAPHIR (by invitation), Chicago.

Numerous investigators recently have reported favorable results in the treatment of undescended testes with gonadotropic hormone. A great deal of justifiable skepticism has arisen, however, as regards the value of this form of treatment in unselected cases. In cases in which there is a mechanical factor that prevents the normal descent of the testes the administration of gonadotropic substance cannot be expected to bring them down.

The excretion of gonadotropic hormone in the urine was studied in 13 cases before and after treatment by Dr. William Saphir of our group, and I am reporting it as an original communication.

It can be stated that the presence of the hormone in the urine of cryptorchids indicates activity of the anterior lobe of the pituitary gland in secreting gonadotropic hormone. The presence of significant amounts of gonadotropic hormone in the urine of cryptorchid children may, therefore, be compared to the increased excretion of gonadotropic hormone which occurs during castration in man. Since in the castrated man and in cryptorchid boys the gonadotropic hormone is presumably of pituitary origin, it seems logical to conclude that the presence of gonadotropic hormone in the urine of the cryptorchids indicates a functionally active pituitary gland. The appearance of the hormone in the urine may, therefore, be ascribed to insufficient activity of the gonads, which fail to modify the hormone or remove it from the blood.

The absence of the hormone in the urine of cryptorchids may be explained by:

1. Pituitary insufficiency, in which case the prognosis following both medical and surgical treatment must be guarded.

2. Functionally active bilateral undescended testes for which endocrine therapy is indicated.

3. Unilateral descended testis functionally active; the undescended testis may or may not be functionally active.

Three boys with unilateral cryptorchidism and ten with bilateral cryptorchidism, between the ages of 5½ and 14½ years, were treated with gonadotropic substance in doses of from 100 to 150 rat units, three times weekly, for a period of from three weeks to four months, the duration of the treatment depending on its success or failure. Determinations of gonadotropic hormone were made before the onset, during the course and three months after the conclusion of the treatment. The method used was Zondek's alcohol precipitation method. According to this method, a minimum of 66 mouse units per liter of urine is demonstrated. A negative reaction, therefore, does not rule out the presence of minimal amounts of the hormone. For practical purposes, however, a negative reaction may be considered an absence of the hormone, although it is realized that traces of the hormone may be present.

On the basis of the findings just mentioned the 5 boys with bilateral cryptorchidism who showed an increased excretion of gonadotropic hormone may be regarded as patients in whom the gonadal mechanism had failed to function but in whom the pituitary gland was still active. The administration of gonadotropic substance to these patients resulted in descent of the testes and the development of other signs of gonadal stimulation. Following the establishment of gonadal function the excretion of gonadotropic hormone returned to the level below which it could not be demonstrated by the Zondek precipitation method.

The 8 patients, 3 with unilateral cryptorchidism and 5 with bilateral cryptorchidism who did not excrete gonadotropic hormone before treatment are of particular interest. The presence of a normal testis in the 3 with unilateral cryptorchidism must be interpreted as indicating the presence of a normally functioning pituitary gland. It was not surprising, therefore, to find an absence of gonadotropic hormone in the urine.

The failure of 2 of the 3 patients with unilateral cryptorchidism to respond to treatment is attributed to the presence of a mechanical obstruction. In the other patient with unilateral cryptorchidism the administration of gonadotropic substance was followed by descent of the testis into the scrotum. Unquestionably, there was no mechanical obstruction, and the success of the therapy might be explained by stimulation of an underdeveloped testis. Three patients with bilateral cryptorchidism who showed no clinical evidence of pituitary dysfunction and who did not excrete gonadotropic hormone in the urine responded rapidly to treatment. The testes descended well into the scrotum in six, four and four weeks, respectively. In these cases there was no mechanical obstruction, and evidently the undescended testes were sufficiently developed to utilize the gonadotropic hormone from the blood, with stimulation and descent following therapy.

The absence of the gonadotropic hormone in the urine of 2 of the 5 patients with bilateral cryptorchidism may be interpreted as indicating a primary pituitary dysfunction, as both patients (patients 5 and 10) revealed clinical evidence of infantilism. In these the administration of gonadotropic substance failed to bring the testes down.

The position occupied by the testes in their relation to the inguinal canal has been unrecorded in most clinical reports. It is to be expected that such findings must of themselves give some clue as to the possibilities for future physiologic development in the light of the newer knowledge of the effect of temperature on testicular function.

The most striking results were obtained in preadolescence and adolescence. On the basis of our limited experience we believe that in the cases of endocrine dysfunction associated with cryptorchidism endocrine therapy is indicated, even at an early age. This is possibly best given at intervals, with regular clinical observation.

In view of these findings we believe that in many instances the test for the presence of gonadotropic hormone in the urine is valuable both in determining the type of treatment and in making a prognosis. The following classification is presented preliminary to a further study of the problem.

Endocrine Therapy Is Indicated in Cryptorchidism

A. If hormone is found in the urine

Bilateral Cryptorchidism. Signs of so-called adiposogenital dystrophia are frequently present. This is the type of cryptorchidism that responds most readily to treatment.

Unilateral cryptorchidism. In this condition the scrotal testis is usually functionally inactive.

B. If hormone is absent in the urine

Bilateral Cryptorchidism. This could be due to: (1) anterior pituitary insufficiency or (2) functionally active undescended testes.

Unilateral Cryptorchidism. In this condition the scrotal testis is usually functionally sufficient.

In both these groups a trial course of hormone therapy should be instituted before surgical intervention is undertaken.

Surgical Therapy Is Indicated in Cryptorchidism

A. If hormone is found in the urine

Bilateral Cryptorchidism. Operation is indicated in otherwise normal boys with clinical evidence of mechanical obstruction. It should be preceded and followed by endocrine therapy.

Unilateral Cryptorchidism. Operation is advisable if the scrotal testis is functionally inactive. If endocrine therapy is unsuccessful surgical intervention should be instituted in an attempt to save the undescended testis.

B. If hormone is absent in the urine

Bilateral Cryptorchidism. If endocrine therapy fails one should operate for anatomic restoration and follow this procedure with endocrine therapy. The functional effect is doubtful if the condition is due to pituitary insufficiency.

DISCUSSION

DR. FREDERIC H. BARTLETT, New York: In conversation with Dr. Bruce Webster, of New York, this week my associates and I formulated indications for the medical treatment as well as the surgical treatment of undescended testes. This statement is not dogmatic. We offer it as a tentative plan.

It seems best that treatment should be started perhaps at 4 or 5 years of age. The technic of treatment is important. One child received twenty-four treatments each day with the exception of Sunday. In that child the testes, which were in the canal and could not be expressed into the scrotum at the start, came into the scrotum as a result of medical treatment.

The indications for surgical treatment have been covered by the paper just read. After a course of treatment in which the technic has been carried out adequately and the testicle has not descended into the scrotum, if the testes cannot be expressed through the external ring it is presumptive evidence that there is an obstruction, and the chances are that the testes will never descend.

This past week my associates and I were confronted with the problem of an undescended testicle which had come down as a result of treatment but which could not be expressed through the abdominal ring. An operation was done on a 6½ year old child. The testicle was successfully implanted into the scrotum in one operation.

This suggestion as to early operation in case of inability of the testicle to be transplanted properly as the result of hormone therapy is worth considering. Certainly the use of gonadotropic substance at the period of puberty carries with it perhaps certain hazards in the nature of precocious development.

DR. HAROLD C. STUART, Boston: Dr. Bartlett in his discussion made one or two references to age, but Dr. Hess did not mention any differences in age. I wonder whether Dr. Hess would care to make any remarks which might modify his statements about the presence of gonadotropic substance in the urine or about the therapeutic indications on the basis of differences of age.

DR. CHARLES HENDEE SMITH, New York: I have wanted for a long time to ask some questions of some one who has been treating undescended testes with hormone therapy. The first thing that I want to know is what cryptorchism is. None of the writers I have read have stated whether they meant true cryptorchism, in which the testes remain inside the abdomen, or whether they were discussing the type in which the testes lie in the region between the external inguinal ring and the upper aperture of the scrotum. The condition must be quite different.

It has always been a dictum that the intra-abdominal testes, even if brought down, do not function. I do not know whether that is still true in the light of the hormone therapy. I do know that there are a large number of children in and about New York whose testes lie in the region between the external ring and the superior aperture of the scrotum. In these the testes can be pushed into the scrotum with great ease. Often they descend into the scrotum if the child lies down and relaxes, if slight pressure is applied to the pubic region. At puberty testes of this type come down if let alone.

A great deal of hormone is being given today over long periods and at great expense to children just before puberty in whom the testes would come down spontaneously, judging by the fact that the testes of most children with this condition do come down without therapy.

I recently observed an amusing case of a child who was refused life insurance because of undescended testes. In the erect position his testes were retracted out of the scrotum but on the table could be easily pushed down and stayed there after he relaxed a little. That child was threatened with, and almost subjected to, an expensive long course of treatment with hormone, I think, without justification.

DR. HERBERT WILLY MEYER, New York: I wish to thank the Council of the American Pediatric Society for the courtesy extended to me, not a member, to enter into this discussion.

My associates and I have always been interested in the question of undescended testicles, and the paper read by Dr. Hess, as well as the discussion that has taken place, has presented entirely the view that so many hold.

My associates and I also feel in our experience at the Lenox Hill Hospital in New York that perhaps gonadotropic substance is given too frequently and too early. If a small amount of daily traction on the ectopic testicle is made by the patient's mother in early life the testicle can be pulled down into the scrotum, and when puberty comes it will stay there. However, there are other types of true ectopic testicles which need gonadotropic substance in order to bring them down into the scrotum.

What surgeons are especially interested in is the question of true undescended testicle, even within the abdominal or outside the internal abdominal ring, held there by mechanical means. It is these that pediatricians see so frequently and in connection with which surgeons feel that they can assure a perfect result in almost every instance, a result in which the testicle will lie at the bottom of the scrotum. If after two or three years the testicle lies against the pubic bone high in the scrotum, the result is poor. Unless one uses the better type of operation one will not get a good surgical result. That is the reason so many pediatricians give so much gonadotropic substance in an attempt to get better results without operation, as surgery, in their opinion, in many instances does not give good results unless the Torek type of orchiopexy is used.

I should like to show a few slides of the Torek operation used at the Lenox Hill Hospital since 1905. The principles are old, and this is the one operation which has given uniformly excellent results. Since its republication by the author in 1926 it has been accepted by almost all surgical clinics all over the country.

(Slides were shown.)

Dr. Julius H. Hess, Chicago: The thought behind this work is what all the members had in mind, I am sure. We have been trying to get away from the excessive and unnecessary use of endocrine therapy, to put it on something like a rational basis. The presence of gonadotropic substance in the urine indicates that the anterior lobe of the pituitary is functioning and the testicles are not. Many of the patients who present this laboratory finding show clinical evidence of obesity and various other signs of adiposogenital dystrophia. In those cases we have seen striking results. Most of the patients respond readily to endocrine therapy. Those are cases in which one would not wish to operate, because the operation would not restore testicular function.

As to Dr. Stuart's question regarding the age at which one finds gonadotropic substance in the urine, one of these patients with obesity was 7 years of age. He responded to endocrine therapy. Most of our patients were from 10 to 15 years of age.

On the other hand, the 2 boys who were normal and in whom there was descent of the testes in four weeks were 5½ years of age.

As to Dr. Smith's question, what is cryptorchidism, it will probably be recalled that I said that one of the things which stands in the way of any set formula for the treatment is the fact that one never knows which testis will come down and which will not. One also knows that many of the conditions of the group of adiposogenital dystrophias are probably pituitary dysfunction, in which recovery may occur spontaneously at or near puberty. It is, however, undesirable in this type of child to wait from five to ten years for nature to bring about the uncertain change, if therapy will accomplish the descent and give hope for increased testicular function in a few weeks. In recording one's cases one should specifically state the location and mobility of the testes, as that is the only way one can draw final conclusions as to which group of conditions justify endocrine therapy.

Dr. Meyer, I am sure, has had remarkable results, but, unfortunately, in Chicago one does not always see results which are as good. In those cases in which the testis is not brought down and held in the young person one frequently sees improvement after operation with the use of further endocrine therapy.

In regard to overstimulation in the patients whom we have treated, we have not seen any condition resembling that due to overstimulation of the genital tissues.

I should like to show two slides in counterpart to what was shown in the way of surgical intervention, to illustrate the physical changes in stature with increased development and descent of the testes following endocrine therapy.

(Slides were shown.)

Meeting at Bolton Landing, Lake George, in 1905. Dr. Linnaeus E. La Fétra, New York, recorder and editor at that time.

Thirty-one years ago at the invitation of the first president, Dr. Jacobi, the seventeenth annual session of the American Pediatric Society was held at this place. Most of the members arrived at Bolton Landing by lake steamer from the city of Lake George. Of a total membership of 50, 29 were present at the meeting, and 5 of these are here today—Dr. Abt, Dr. Kerley, Dr. Morse, Dr. Shaw and I. The sessions were held in the original Sagamore Hotel, which burned some years ago, and in Dr. Jacobi's delightful home.

A reading of the twenty-seven papers and of their discussions reveals much of interest and emphasizes the great advances in the knowledge of pediatrics during the years that have elapsed. The majority of the papers were clinical or clinicopathologic, though some were presentations of laboratory studies, particularly of the urine and of the blood counts in various conditions. The president's address by Dr. C. G. Jennings dealt with the comparatively new subject of the medical supervision of schools and school hygiene. Medical school inspection was established in Boston in 1894 and in New York in 1897.

The meetings of those early days were generally enlivened by heated and acrimonious discussions of infant feeding. The percentage method so warmly advocated by Dr. Rotch, by which the fats, sugars and proteins could be changed

quantitatively and relatively was pitted against simple dilutions of whole milk. Algebra was called in to aid in the construction of the baby's formula, and there were heated debates over such formulas as 2-6-1 and 3-6-1.25. Calories as yet played little part in the calculations. Eiweiss milch and the different types of acid milks had not been developed.

Among the papers presented, Dr. Hand analyzed 145 cases of typhoid fever. How difficult it has been of recent years to show students examples of that disease in children! Dr. Saunders made a plea for earlier intubation in diphtheria. At that time many pediatricians gained quite an income from practicing the procedure, but nowadays, with active immunization against diphtheria, which we owe to Dr. Schick, intubation is seldom needed. It would be interesting to know whether any one here has performed an intubation in the past year. Dr. Townsend reported a case of intestinal and peritoneal tuberculosis. It is interesting that the tuberculin test was not used because the patient had a constantly elevated temperature. Thus this was before the introduction of the early skin test with tuberculin and even before Calmette's conjunctival test, which was used with much misgiving and opposition. The doctrine of allergy with its multitudinous applications was yet embedded in the mind of Pirquet.

Scurvy was known to be due to a deficiency disease and to be cured by citrous juices, especially orange juice, but the vitamins had not been brought out by Cassimer Fink.

Stenosis of the pyloris was a condition well recognized, but surgical treatment was still in the dark ages of gastro-enterostomy. The simple and safer method of slitting the tumor longitudinally, which was successfully practiced by Downes and others, had not yet been devised.

New members elected were Drs. Howland, Southworth, Ruhräh and Knox. Among the honorary memberships, one was accorded to Dr. Osler. It is interesting that the honored Sir William of later days was the fourth president of our society in 1892.

The great charm of the meeting was, of course, Dr. Jacobi's warm-hearted and gracious hospitality. Even the humblest member, such as myself, was treated as an equal and welcome colleague. Dr. Jacobi was at his best when entertaining his pediatric friends, either in his magnificent library on Thirty-Fourth Street in New York, opposite what is now Macy's, or in his country home.

We today are fortunate in being able to survey the many milestones of progress made since our last meeting here. When in another thirty years some of us return to this place, now hallowed for us as a shrine in honor of our first president, there will have been, no doubt, still greater advances. May the American Pediatric Society continue to hold its place in the vanguard of pediatric progress!

(Lantern slides of members present at the 1905 meeting were shown.)

Final Session

Saturday Evening, June 13

MEDITERRANEAN DISEASE — THALASSANEMIA (ERYTHROBLASTIC ANEMIA OF COOLEY). DR. GEORGE H. WHIPPLE (by invitation), Rochester, N. Y.

This paper was published in full in the *Journal of Pediatrics* (**9**:279, 1936).

A PATIENT WITH CONGENITAL HEART LESION WITHOUT CYANOSIS OR SUBJECTIVE SYMPTOMS, SHOWN AT THE MEETING IN 1905 AND SHOWN TODAY. DR. HENRY L. K. SHAW, Albany, N. Y.

I am very proud of the fact that I was privileged to attend the 1905 meeting of the American Pediatric Society on this very spot. At that meeting I presented a 6 year old boy with a congenital lesion of the heart without any cyanosis or subjective symptoms. I brought this young boy and his mother to Bolton Landing.

and the members examined him. Various opinions were expressed as to the location of the cardiac lesion. They all agreed on one point; that was that unless the boy lived a very careful life he would not live more than a few years.

Today I am presenting the same patient, who is now a man 35 years of age. He is strong and healthy, has never restricted his method of living and works daily on the railroad. He is married and has 3 children.

The cardiac thrill and loud murmurs are just as distinct as they were thirty-one years ago. I present him on this occasion to show how little one really knows about the prognosis of a congenital cardiac lesion. The man is healthy and active today, while most of those who gave such an unfavorable prognosis have themselves passed away. I have a roentgenogram and an electrocardiogram which I think the members will be interested in seeing. The first time that the patient was presented nothing was known about roentgenograms or electrocardiograms.

ANEMIA OF THE NEW-BORN: REPORT OF A CASE WITH ESPECIAL REFERENCE TO THERAPY. DR. E. J. HUENEKENS, Minneapolis.

A case of anemia of the new-born is reported in which the condition yielded to treatment by intramuscular injections of liver extract. While there is a tendency in this disease toward spontaneous gradual cure, the sudden dramatic improvement in this case makes plausible the specific effect of liver. A similar condition exists in the macrocytic anemia of pregnancy, in which there is temporary absence of the intrinsic factor. This disease is cured by liver extract and does not recur after the injections of liver are discontinued. The similarity between the macrocytic anemia of pregnancy and the anemia of the new-born is striking, and it is possible that there is some relationship between the two. In future cases of anemia of the new-born it should be possible to prove the temporary absence of the intrinsic factor and the specificity of liver therapy by tests on animals with the gastric contents of the infant.

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METABOLISM AND EXCRETION OF BILE PIGMENT IN ICTERUS NEONATORUM. DR. S. G. ROSS, DR. T. R. WAUGH (by invitation) and DR. H. T. MALLOY (by invitation), Montreal, Canada.

The investigation reported was an attempt to elucidate which of the three main factors in the production of jaundice, namely, excessive hemolysis, impaired liver function and obstruction in the biliary tract, is at work in the production of icterus neonatorum.

The work was carried out along three lines. A group of infants, with and without jaundice, were studied on the first and fifth days of life. The blood was examined for the following: the red cell count, the concentration of hemoglobin, the total corpuscular volume and the bilirubin content. As was expected, the bilirubin content was much higher in the patients with jaundice. In both groups there was a reduction of about 10 per cent in the number of red blood cells, in the concentration of hemoglobin and in the total corpuscular volume. These findings suggest that an equal degree of hemolysis had taken place in both groups and are brought forward as evidence that excessive hemolysis alone is not the factor on which the development of jaundice depends.

In the second investigation studies of the blood were made on a group of 63 infants at the age of 4 or 5 days, the period at which jaundice is usually most intense. The examination of the blood included tests to determine the concentration of hemoglobin, the total corpuscular volume and the van den Bergh reaction. At the same time samples of urine were examined for bilirubin. The concentration of hemoglobin was slightly higher in the group with jaundice, and the figures for total corpuscular volume in the two groups were almost identical. These findings do not support the view that excessive hemolysis had taken place in the patients with jaundice.

None of the patients showed a prompt direct van den Bergh reaction in the blood. This finding is generally felt to be incompatible with the presence of true

obstructive jaundice. The indirect van den Bergh reaction showed an average of about 10 units in the patients with jaundice and of about 4 units in the patients without jaundice.

Examination of the urine showed that bilirubin was almost constantly present in the patients with jaundice. Therefore, the jaundice did not depend on the presence of the promptly and directly reacting pigment in the blood and thus was not due to an obstructive factor. Bilirubin was absent in practically all the infants without jaundice.

The third series of observations were made on a group of 35 infants over the first seven days of life. A quantitative estimation of the urobilin and bilirubin (including biliverdin) in the stools was made, also an estimation of the urobilin and bilirubin contents of the urine. The examination of the stools showed a relatively high excretion of urobilin for all the infants. The total excretion of bile pigment—urobilin and bilirubin (including biliverdin)—was greater in the patients without jaundice. In a purely hemolytic type of jaundice the reverse would be expected. The inference is that one of two factors must be operative here—either dysfunction of liver cells or obstruction in biliary channels. The previous investigation appears to rule out the obstructive factor. By exclusion, therefore, it appears that the liver cells are at fault.

The excretion of urobilin in the urine was above the normal in both groups. It was higher in the group without jaundice, just as in the stools. All the patients with jaundice showed bilirubin in the urine, whereas only 5 without jaundice showed bilirubin in the urine (and that only in traces).

The findings suggest that icterus neonatorum depends on two factors: the primary basic factor of excessive hemolysis and a second deciding factor—a functional disturbance in the excretory mechanism of the parenchymal liver cells in this period.

DISCUSSION OF PAPERS READ BY DR. WHIPPLE, DR. HUENEKENS AND DR. ROSS

DR. IRVINE MCQUARRIE, Minneapolis: I should like to refer to the case of an older child observed at the University Hospitals during the past year who presented a picture not unlike the one reported by Dr. Huenekens. This case strongly suggested that a pernicious anemia-like picture may occur as a temporary functional disturbance, which is amenable not only to relief but apparently to complete cure.

A girl 10 years of age was found to have severe anemia. No antecedent etiologic factor was apparent. Her hemoglobin was about 20 per cent. She had a blood picture of pernicious anemia, with macrocytosis, hyperchromia, anisocytosis, poikilocytosis and changes in the white cells fairly typical of pernicious anemia in adults. The reticulocyte count was very low. She responded to transfusion, but the response lasted for less than a week, after which the hemoglobin content fell from 39 to 24 per cent.

My associates and I found on further examination that she had a very smooth, sore tongue, which was beefy red. She complained of mild paresthesia in the hands and feet. She had persistent achlorhydria, no free hydrochloric acid being secreted even after the injection of histamine. The gastric contents had no effect on the blood picture of experimental rats, when injected subcutaneously. In other words, the patient appeared to have the picture of pernicious anemia identical with that seen in adults. It is known how rare pernicious anemia is in children.

When liver extract, which contains the antipernicious anemia factor, was administered, the reticulocyte count rose to 21 per cent after the first dose. The hemoglobin and red cells were regenerated rapidly. The picture tended to return to normal within a short time, probably a month, as I recall, after which the extract was discontinued. The paresthesia disappeared; the gastric contents returned to normal, and the lingual papillae were regenerated.

DR. C. E. SNELLING, Toronto, Canada: The suggestion was presented in regard to the treatment by liver extract of conditions that are probably related to erythroblastosis, such as anemia of the new-born. In Toronto my associates and I are

very pessimistic about the treatment of the group in which there is definite jaundice. We have had some 13 cases in the last three or four years; 5 patients have recovered. One is alive and well at the present time. One died of streptococcic septicemia, and the other 3 showed kernicterus associated with retraction of the head, diplegia and marked mental retardation.

With reference to Dr. Ross' paper, the work of Goldbloom and Gottlieb and Anselmino and Hoffmann in Germany was an outstanding advance in explaining why the red cell count of the blood fell from the high level at birth to the lower level, but it is difficult to conceive why the liver, if it is functioning normally at the early period, cannot excrete the hemoglobin that is destroyed at that period.

Work such as that of Rich and of Mann and Bollman showed that the liver will excrete all the hemoglobin that is normally broken down if only 5 per cent of the organ is left. Also, Hess was unable, with a duodenal tube, to obtain any bilirubin by extracting the contents of the duodenum of infants in the first few days of life. The fall in the red cell count of the blood is gradual; the level does not drop suddenly but continues to drop over a period of two weeks. At birth the bilirubin content is above normal and continues to rise for a period of four or five days up to a week and then falls.

It was also observed that at that time there was a histologic change in the liver. Histologic observation of the liver up to the period of four or five days showed that the reticulo-endothelial cells were of a different type than the cells of a later period or those seen in adults, and we wondered whether that had any connection with the production of the bilirubinemia. We made no measurement of the bile pigment in the urine and made no estimation of the degree of clinical jaundice in the cases that we studied. The fact that Dr. Ross found bile present in the urine in association with a negative direct immediate van den Bergh reaction was an interesting point and one which made one wonder what the mechanism was.

Dr. Alfred H. Washburn, Denver: In regard to Dr. Huenekens' paper, I should like to express a word of caution about the interpretation of the results of liver therapy in the early weeks or months of life. There are several factors that should make one extremely cautious in interpreting the results. The first of those factors is the possible occurrence in either healthy or anemic infants of rather sudden jumps in the reticulocyte count followed by sharp rises in the red cell count without therapy of any type.

The other factor which should make one cautious is the extreme amount of error possible in the technical procedures involved in taking the red cell count and, especially, in taking the reticulocyte count.

Dr. George H. Whipple, Rochester, N. Y.: I do not suppose that it is proper for a laboratorian to ask any questions about these clinical reports, but they interested me very much, and I was wondering what effect other types of liver fractions might have on these interesting pseudopernicious anemias in infants. There are other liver fractions available beside the pernicious anemia fractions, distinct and separate, some of them potent in secondary anemias due to loss of blood. If one had the temerity it would be interesting to see what the reaction might be. One realizes, of course, the limits of clinical responsibility relative to the icterus of the new-born. I have always had a great interest in that condition, as I worked with icterus in animals for many years.

To establish definite evidence of disturbed liver function is extraordinarly difficult.

In this connection I wondered whether it might be possible to test with bile salts given by mouth the physiologic response. Bile salts have a definite influence on liver function, I believe, and certainly they have much to do with the renal metabolism.

Dr. E. J. Huenekens: I agree with Dr. Washburn that one should not draw too many conclusions from therapy of this kind, especially on the basis of the findings in only one case. However, in reading over the literature on anemia of the new-born, I noted that while many patients recovered spontaneously or with

some other form of therapy, the improvement was very gradual, taking place over a period of months, and not so dramatic as in the case which I reported. I think that the only way that one can prove anything is to take the contents of the stomach in future cases of this kind and test for the intrinsic factor.

All that I hope to do in my paper is to stimulate physicians to perform in future cases that experiment which should help settle the etiology of this disease.

INTRAVASCULAR CLOTTING IN ABANDONED FETAL CHANNELS IN THE NEW-BORN. DR. W. A. MULHERIN and DR. JOSEPH KRAFKA (by invitation), Augusta, Ga.

The hypothesis is advanced that increased coagulation time, which is noted in early infancy, is not incidental but that it exists as a part of a natural mechanism which provides against thrombus formation during the period when the abandonment of fetal channels would constitute a serious embolic threat. We believe that the hypothesis correlates a whole series of hitherto obscure and isolated events: (1) increased coagulation time, (2) bilirubinemia, (3) time of dropping of the cord, (4) time of abandonment of the fetal vascular channels, (5) the absence of thrombi in such channels and (6) the absence of emboli except in cases in which infection exists.

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CHARACTER OF THE BLOOD CLOT IN NORMAL PERSONS AND IN HEMOPHILIACS. DR. CHARLES F. MCKHANN, DR. F. T. CHU (by invitation), DR. ARDA A. GREEN (by invitation) and DR. R. CANNON ELEY (by invitation), Boston.

A normal blood clot is a firm gelatinous mass containing structural webs or meshes of fibrin. The clot slowly retracts, exuding serum, but even after retraction retains within its substance a considerable amount of water bound in gelatinous material. Variations from this normal clot are observed. One extreme is the loose, thready or meshy clot, rapidly retractile, with little gelatinous material, which permits the escape of much of the contained water and which holds only part of the formed elements within its meshes. Such a clot might be termed hydrophobic and is found typically in hemophilia. The other extreme is the gelatinous, almost structureless clot with very few threads of fibrin, which retracts slowly, if at all, and which exudes little serum. Formed elements appear to be bound in the clot by its jelly-like structure and, to a less extent, by the meshes of fibrin. Such clots might be described as hydrophilic. They are found normally in invertebrates and, to a varying degree, in certain types of purpura.

The influence on the type of clot of the various substances involved in the process of coagulation has been investigated by means of in vitro experiments.

It has been ascertained that within a wide range, extending well beyond physiologic limits, the amount of fibrinogen present is not the important item in the type of clot which is formed. Salts, especially calcium, were found to exert no influence within concentrations well above and below physiologic levels, nor was hydrogen ion concentration an item within the range of p_H 5.4 to 9. The type of clot was dependent only partly on the amount of thrombin present, although this did affect greatly the speed of coagulation. The factors which seemed most to influence the hydrolability of the clot were the amount of tissue substance and the number of blood platelets present. The addition of small amounts of tissue extract not only accelerated coagulation but resulted in the formation of large, firm, less retractile, i. e., more hydrophilic, clots

As blood plasma and even the purified fibrinogen used in biochemical research have been in the process of preparation contaminated with the débris of blood platelets, the influence of these elements was sought in experiments utilizing citrated plasma which after chilling had been passed through a Seitz filter. Such plasma, when recalcified, clotted poorly, if at all. The addition of blood platelets led to slow coagulation which required a period of several hours and resulted in the formation of typical hydrophobic, rapidly retractile clots, strikingly similar in rate of coagulation and in appearance to the clots of hemophiliacs. The addition

of tissue extract to the filtered plasma produced no true clot but led to the formation of a heavy flocculant precipitate. The addition of both platelets and tissue extract led to coagulation within a few minutes, with the formation of large firm, slowly retractile normal clots. From these results it would seem that the platelets influenced retraction, that tissue extracts influenced hydration but, if added in excessive amounts, especially in the absence of platelets, resulted in the loss of the hydrating capacity and the suppression of true clotting.

Although the plasma of hemophiliacs was clotted rapidly by purified thrombin or by snake venom, a normal clot was not obtained, but the typical hydrophobic, loose-meshed, quickly retractile clot developed. The addition of tissue extract to the plasma of hemophiliacs not only increased the rate of coagulation but resulted in the formation of large, firm, slowly retractile hydrophilic clots. If larger amounts of tissue protein were added, the clots became very hard and firm and did not retract.

Those patients with hemophilia who received extract of placental tissue by oral administration and who evidenced a reduction of the coagulation time of the blood also showed definite improvement in the type of the clots formed, but in no instance has it been possible with the dosage employed to secure the formation of entirely normal clots.

DISCUSSION

Dr. A. A. Weech, New York: These findings by Dr. McKhann and his associates are peculiarly interesting to several of us at the Babies Hospital, for they may help to explain a phenomenon which has been observed over several years in our experimental work. The phenomenon has to do with the nature of the clot which develops in lymph.

When a cannula is inserted into one of the lymphatics of the leg of a dog there is no flow of lymph from the cannula so long as the leg is motionless. When the stimulus for the flow of lymph is supplied by normal activity, such as walking, clear lymph flows freely from the cannula and can be transferred to tubes. The clot which forms in this lymph is usually fine and contracted and resembles somewhat the film which forms in spinal fluid in tuberculous meningitis. If, however, the stimulus for the flow of lymph is supplied by massage instead of by normal activity, the lymph which is collected shows an entirely different type of clot. The clot is more voluminous, and it contracts poorly, so that the clearness of the entire sample is obscured by a gelatinous opalescent mass.

Our first impression on observing this was that we had here encountered wide and unreasonable variations in the fibrinogen content of lymph; we were led to suspect that fibrinogen was being added to the lymph from the tissues by the stimulus of massage. It was difficult to believe that the apparent increase in fibrinogen came from the blood stream, since there was no associated change in the other protein fractions, that is, in the albumin or in the globulin. The findings which Dr. McKhann has presented suggest a more reasonable explanation for the phenomenon; it is possible that massage adds tissue extract and not fibrinogen to the lymph. The tissue extract would not only change the character of the clot so as to make it appear larger but would also increase its bulk by contributing to its nitrogen content.

Dr. Thomas B. Cooley, Detroit: I have been intensely interested in the work of Dr. Khann, which I think is throwing light not only on the question of hemophilia but on the whole vexing problem of the clotting of the blood. I was particularly interested in the demonstration that there is need for interaction between platelets and tissue juice and that one cannot assume, as some have, that these have practically the same action.

My associates and I have been approaching these problems from a different angle, and I might mention one or two of our findings which seem to me to fit in rather well with those of Dr. McKhann. For one thing, though it has been generally assumed that the platelets' content of cephalin plays an important part in the initiation of the clotting process, we have been able to find so little cephalin by analysis of platelets that it would seem that if it is really important it must be derived from tissue juice.

Dr. McKhann's work may throw some light on another matter which has troubled us. We have been using an extract of a different source and type from that used by McKhann and Eley for the treatment of hemophilia and have had clinical results comparable with theirs, except that we do not get the reduction in the clotting time that they do. It may be that we get a clot of better quality, even though it is slow in forming.

UTILIZATION OF IRON. DR. PEARL SUMMERFELT, Toronto, Canada.

Iron must be present in the ingested food for absorption to take place. Before absorption of iron can take place the iron must be present in such a form that it can go into solution during the digestive process, and in addition the soluble iron must be present in a soluble ferrous form.

By means of artificial gastric digestion which simulated conditions present in the upper gastro-intestinal tract of children in vitro digestions were done on various foods. The greatest amount of soluble iron was found in vegetables and fruits and the least in eggs and meat. It was shown by means of regeneration of hemoglobin in anemic rats that food fed on the basis of its soluble iron content was a closer measurement of the utilization of iron in three of the foods tested than when rats were fed the same amount of iron on the basis of the total iron content of the food.

The proportion of iron reduced to the ferrous state was studied, and it was found that the percentage of ferrous iron varied in different foods. This was dependent on factors such as precipitants and reducing substances in the food and the acidity of the gastric contents.

DISCUSSION

DR. GEORGE H. WHIPPLE, Rochester, N. Y.: Iron therapy appears to be so delightfully simple that it seems that there could be no misapprehension or differences of opinion regarding it. Yet those who have had even a mere cursory acquaintance with the literature on this subject will realize that there are acute differences of opinion and that no two persons can agree in all the details relative to this subject.

It is not surprising, therefore, that I cannot agree with the opinions expressed in this paper relative to iron, and I know there are other persons of eminence who would disagree with both of us. So one sees that this is a field of acute differences of opinion.

All the experiments carried out by my associates and me have dealt with dogs. Dogs may differ from rats, of course, and man may differ from both dogs and rats, which introduces another factor.

The anemia in these experiments I take to be a nutritional anemia, whereas the anemia in our experiments is that due to loss of blood. In our experiments on subjects with anemia the introduction of iron intravenously is the only method by which one obtains the full response. Then one gets a quantitative return. For every 3.3 mg. of iron one obtains a return of 1 Gm. of hemoglobin in due time. I think that the data are adequate to support that statement.

When one feeds iron, any kind that one chooses, a number of things may happen. We have been unable, when feeding ferrous, ferric or other iron salts, to get back more than 40 per cent of that iron as new hemoglobin, no matter what diet was given, no matter how complete the exhaustion of the stores of iron was and no matter what salt or what combination of salt and foods was given. As the amount of iron given by mouth is increased its return as hemoglobin falls off.

DIETARY PROTEIN AND HEMOGLOBIN FORMATION: AN EXPERIMENTAL STUDY. DR. A. A. WEECH, DR. M. WOLLSTEIN and DR. E. GOETTSCH (by invitation), New York.

Dogs maintained on a diet deficient in protein exhibit an initial rise and later a progressive fall in the concentration of hemoglobin in the blood. Measurements on 4 dogs showed that the change in the hemoglobin content ran approximately

parallel with the changes in the red cell count and in the relative volume of the red cells (determined by the hematocrit). The average percentage volume of red cells for 21 dogs during continued maintenance on the diet was: initial, 46.6; after twenty days, 48.6; after forty days, 46.1; after sixty days, 41.0; after eighty days, 37.0; after ninety days, 33.7. Measurement of the total volume of red cells in the circulation showed that the decline in the hemoglobin content was continuous from the time of starting the diet. After ninety days the total volume of the circulating erythrocytes averaged about half of the original volume. The average finding for 10 dogs in terms of cubic centimeters of red cells per kilogram of initial body weight was as follows: initial volume, 43; volume after twenty days, 39; volume after forty days, 35; volume after sixty days, 29; volume after eighty days, 26; volume after ninety days, 23. The measurement of the total amount of plasma in the circulation disclosed a rapid fall during the first twenty to thirty days to a volume which was then maintained for the duration of the experiment. Because the early decreases in circulating volumes affected both the plasma and the erythrocytes, the red cell counts and determinations of hemoglobin made in the usual manner failed to record the progressive loss from the circulation.

In a larger series of 37 dogs similar measurements made initially and after three weeks of maintenance on the diet confirmed the findings in the smaller series. The average hematocrit reading increased from 46.7 to 49.0 per cent; the average plasma volume decreased from 891 to 761 cc.; the average volume of the erythrocytes declined from 793 to 744 cc. These changes were shown to possess a high degree of statistical significance.

The diet furnished about 2.4 mg. of iron per kilogram of body weight per day. In one experiment the addition to the daily food of 11 Gm. of liver extract failed to prevent the changes described as characteristic for the entire series. The conclusion is therefore justified that the failure of normal hemoglobin formation resulted from deficiency of protein alone.

Since the loss of hemoglobin in patients on the low protein diet is definitely demonstrable in as short a time as three weeks, there is no evidence in the experiments of a reserve supply either of hemoglobin or of precursors of hemoglobin which can be utilized to maintain a constant amount in the circulation. The experiments do not exclude the possibility that reserves may be available which can be called on to assist in recovery after hemorrhage. If such reserves do exist the experiments suggest that they are depleted concomitantly with the circulating hemoglobin.

The findings in this study have a practical significance. Many patients with illness of relatively brief duration experience anorexia and show a moderate decrease in the level of albumin in the serum. The absence of a decline in the red cell count or in the percentage of hemoglobin has usually been attributed to a "hemoglobin reserve." Because decreases in the serum albumin content are associated with decreases in the plasma volume, it is probable that these patients actually do lose circulating hemoglobin and that the loss is merely masked when measurements of the concentration are the only criteria.

DISCUSSION

DR. MARTHA WOLLSTEIN, Grand Rapids, Mich.: My contribution to this paper was a minor one. I simply supervised the studies on the blood and performed autopsies on four of the experimental animals of Dr. Weech and Dr. Goettsch. One point to be added probably has suggested itself to most of the members; that is, the condition of the bone marrow of these animals. Smears and sections from both the flat and the long bones of all the animals examined were studied.

In three of the four animals the marrow, as far as could be determined, was normal, showing no change which could be detected. In the fourth case there seemed to be a suggestion of mild hypoplasia. I say "seemed" because I was unable to decide whether this was really the case. Therefore it would appear

that the question as to whether under the circumstances of these experiments the marrow is demonstrably changed or influenced cannot be answered until further studies have been made.

DR. IRVINE MCQUARRIE, Minneapolis: I have no comment to make regarding this interesting paper other than to ask a question in regard to one of the slides shown. In connection with the chart showing the partition of the loss of nitrogen I should like to ask Dr. Weech by what means he determined how much came from each of the circulating proteins, that is, globulin, albumin and hemoglobin. Was the loss calculated in each case from the difference between the original and final values, or was there some way of determining how much was being manufactured during the period of observation?

DR. DANIEL C. DARROW, New Haven, Conn.: All the members owe a debt of gratitude to Dr. Weech for so carefully demonstrating the decreases in the volume of the plasma which occur with low values for the serum protein. I have been interested in this subject for a number of years and was able to demonstrate in certain patients who showed the nephrotic syndrome that the decrease in plasma volume was as great in that condition as has been demonstrated in marked dehydration.

I think that this is of special importance, for when one speaks of dehydration one of the theories is that most of the symptoms are produced by the decrease in the plasma volume; yet the patients with marked edema and probably an equally great decrease in the blood volume do not show symptoms characteristic of dehydration.

I think that the findings for the patients with nephrosis tend to show a minimum level for the serum protein. I should like to ask Dr. Weech whether this has not been observed by him and his associates. The plasma protein content in the nephrotic syndrome never goes below 3 or 3.25 per cent.

DR. THOMAS B. COOLEY, Detroit: I do not know why one always interprets such experiments as these as indicating defective hemoglobin formation. I should have read Dr. Weech's chart, in which the changes in the hemoglobin level follow exactly those of the erythrocyte count, as indicating with equal probability failure in the formation of red cells. In other words, the defect could as well be in the structural material for cell building as in the essentials for the synthesis of hemoglobin.

DR. ALFRED T. SHOHL, Mirror Lake, N. H.: Dr. Weech has shown that the several factors that he mentioned act differently. Some are more resistant than others. He also mentioned that with an adequate amount of protein the deficit of hemoglobin did not occur. I wonder whether he has made experiments in which varying amounts of protein were used so that he can state whether the deficiency of serum albumin or the deficiency of hemoglobin comes first or is more easily produced by the deficiency of protein.

DR. GEORGE H. WHIPPLE, Rochester, N. Y.: I do not wish to appear to be discussing every paper. It is only on the urgency of the president that I speak again, for the last time.

I am tremendously interested in the question of the regeneration of plasma and of hemoglobin. I enjoyed immensely the interesting presentation of Dr. Weech. I have been interested in all his papers. He is in a field where healthy and stimulating differences of opinion are developing.

The question of reserve is a difficult one to answer, even when experiments are carried out under the most carefully controlled conditions. The question as to whether the reserve that may be used for building hemoglobin in emergency of depletion of plasma may be used in the regeneration of plasma protein can be approached. I am not prepared to make a definite statement, but there seems to be some possibility of shift and exchanges, as might be anticipated, when both these reserves, or the common reserve, if one chooses, has been depleted, and on a favorable diet one watches regeneration of both proteins and hemoglobin.

My associates and I thought at one time that the plasma proteins took precedence; we are not sure. Both go together. The plasma protein is more promptly returned to normal under such conditions.

The question of the shift of the plasma volume is also interesting, and the pitfalls are many. The methods used are none too good, in spite of all the efforts that have been made, and there is some difference of opinion as to whether the endothelial linings might not be modified by differences of the protein level and therefore introduce a factor of error in the accepted methods for determination of the blood volume.

DR. A. A. WEECH, New York: Dr. McQuarrie wished to know how the last chart was prepared. The chart was presented as only an approximation of the facts, as not all the data were obtained in the same experiments. The total loss of nitrogen during maintenance on the diet was estimated from the results of four experiments to determine the balance; the losses in albumin, globulin and hemoglobin were computed from the average findings in a larger series of experiments in which measurements of concentration as well as of plasma volume and cell volume were available. With regard to the interchange between proteins going on during the experiments, we have no information; we were able to evaluate the initial and end states only.

I prefer not to give a definite answer to Dr. Darrow's question regarding the lower limit of the level of the total serum protein encountered in patients with nephrosis without first consulting our laboratory records. My impression is the same as his, namely, that concentrations under 3 Gm. per hundred cubic centimeters are rare. However, I should like to stress the fact that the changes in the plasma volume in these experiments are correlated with the level of the serum albumin much more closely than with the concentration of the total protein.

Dr. Cooley suggested that the failure of production of hemoglobin in these experiments may have resulted from inability of the animal to manufacture the stroma of red cells rather than from a direct effect of the diet on the protein portion of the hemoglobin molecule. I cannot deny this possibility. However, since the diet is known to produce general depletion of the stores of protein of the body, it is not unreasonable to think that there is also a direct effect on the hemoglobin content. I am not unwilling to believe that the formation of both stroma and hemoglobin are inhibited by the diet.

I cannot reply to the question of Dr. Shohl, since we have not experimented with different levels of protein in the diet.

Dr. Whipple mentioned the difficulty in methods, particularly in the method for determining the plasma volume, and correctly stated that this difficulty should be held in mind in drawing conclusions. It is chiefly because of the error involved in measurements of the plasma volume that we have not presented the results of individual experiments but in every instance have averaged the results of all the available experiments before preparing the charts. I may add that when the results in separate experiments are examined by the statistical method the more important findings in this study are substantiated.

Book Reviews

Williams' Obstetrics. Edited by Henricus J. Stander. Seventh edition. Price, $10.00. Pp. 1,269, with 747 illustrations. New York: D. Appleton-Century Company, 1936.

The first edition of Williams' Obstetrics appeared in 1903. The book immediately attained a commanding position among books on obstetrics and was widely used as a textbook and as a book of reference. It went through repeated editions, the sixth of which, after careful revision, was completed by Dr. Williams in 1930. During the years which had elapsed since the first edition appeared, the book had stood in the first rank of texts in the English language on the subject of obstetrics, if indeed it had not outranked all other books in that tongue.

The present revision was done by Dr. H. J. Stander, Dr. Williams' friend and former pupil. Dr. Stander has to a great extent maintained the form and arrangement of the book while adding needed new material and occasionally revising the old.

The first three chapters, devoted to anatomy and physiology, show no appreciable change. To chapter 4, devoted to the maturation, fertilization and development of the ovum, material taken from the valuable work of Hartman, Corner and Bradley Patten has been added. The chapters on the development of the fetus and the changes in the maternal organism required little change. For the illustration of the fetal circulation in the older book have been substituted the diagrams of Jordan and Kindred, which are much better.

A new chapter has been introduced in which is summarized the available knowledge concerning the "sex hormones" and their relation to menstruation, pregnancy, parturition and lactation. There is an excellent outline of reproductive endocrinology. A brief discussion of this complicated subject, which should be distinctly useful to the student and the practitioner, is given.

To the chapter on the management of normal pregnancy has been added a discussion of the vitamins which have a relationship to reproduction. For Dr. Williams' old list of instructions to expectant mothers has been substituted that in use in the Cornell Clinic. The chapters on the physiology of labor, the forces concerned in labor, the mechanism in face, brow and breech presentation and the conduct of normal labor remain essentially as written by Dr. Williams. Some new illustrations showing the mechanism of the delivery of the head have been introduced in the chapter on the physiology of labor. These are by Elizabeth Broedel and are a distinct improvement over those in the last edition. New illustrations also appear in the chapter on the conduct of normal labor. Those showing the method of repair of perineal injuries are excellent, but one wonders why a double catgut suture should be needed to bring together the vaginal mucosa after all the deeper structures are united.

A distinct addition is the chapter on amnesia, analgesia and anesthesia in labor. A comprehensive review is given of the methods at present available for the relief of the pain of labor. The practitioner will find this distinctly helpful.

The discussion of the puerperium remains essentially as it was. The most notable addition concerns the results of examination of the blood during recovery from pregnancy and labor. The exceedingly clear and simple chapter on forceps, which was one of the valuable features of Dr. Williams' book, has been retained. The discussion of operative obstetrics remains as it was.

A new chapter dealing with diseases of the kidneys and urinary tract has been added. This fulfils a useful purpose, since a considerable amount of information has accumulated on this subject. The material is well summarized, and the reproductions of pyelograms are well chosen.

The chapter on the toxemia of pregnancy has been brought up to date. Dr. Stander has done noteworthy work in this field and is well qualified to give an accurate summary of the available information. This feature of the book is particularly satisfactory.

A great part of the material in the book as it was left by Dr. Williams did not require change. In the parts in which time had necessitated some change or the addition of new material the editor has made such revision or addition as was needed. He deserves great credit for having succeeded in keeping the volume at almost its former size; the present edition is larger by only a little more than a hundred pages. Dr. Williams' many friends and the still larger number of physicians who have been accustomed to regard the book as their obstetrical guide will have no difficulty in recognizing an old friend.

To revise the book of another requires not only the labor demanded by such a task but also a feeling of friendship and devotion to the original author. Dr. Stander has accomplished this task successfully. The book has been rendered capable of additional years of service as a textbook and as a guide for practitioners. Dr. Williams, I believe, would be satisfied with it.

The Nutritive Value of Fruits, Vegetables, and Nuts. By R. A. McCance, E. M. Widdowson and L. R. B. Shackleton. Paper. Price, 2s. net. Pp. 107, with 26 illustrations. London: Medical Research Council, 1936.

The first part of this book contains a detailed account of the authors' method of food analysis, with tables of the various constituents of fruits, vegetables and nuts. Some of the findings are of interest. Vegetables are considered an excellent source of calcium, but except in green leaves they do not usually contain much calcium. The iron in cooked vegetables varied from 0.22 to 4 mg. per hundred grams. Dried apricots, peaches and raisins were high in iron, as well as such fresh berries as cranberries, currants, loganberries and raspberries.

The last part of the book contains data obtained in the study of cooking vegetables. Here some of the findings are surprising. The waste incurred by throwing away water in which vegetables is cooked is small. Conservative methods of cooking vegetables are unlikely to increase the calcium, phosphorus and iron in a mixed diet by more than 3 per cent.

This is an excellent monograph and certainly continues the high standard set by this series of studies.

Pédiatrie Pratique. By E. Terrien. Paper. Price, 24 francs. Pp. 247. Paris: Masson & Cie, 1936.

Beginning with pulmonary abscess and ending with xanthomatosis, the author discusses eighty-eight subjects from the standpoint of therapeutics. His expositions are brief, but readable and up to date. A cross-index by systems is included. This is an interesting little book on pediatrics from the French point of view.

Daily Log. By Dr. John B. Colwell. Price, $6. Pp. 494. Champaign, Ill.: Colwell Publishing Company, 1936.

The 1937 edition of this useful book for the keeping of the physician's accounts has the usual spaces for recording and is arranged for daily records. It should be of great help to the doctor in systematizing his accounts.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4: 30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York: Time: June 3, 4 and 5, 1937.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: University, Va. Time: April 29-30 and May 1, 1937.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Atlanta. Time: December 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Milo K. Miller, 122 N. Lafayette Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Edwin A. Socola, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.
Place: Houston. Time: Fall, 1936.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Secretary: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Thurman B. Givan, 115 Remson St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Robert Black, Del Prado Hotel, Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. I. T. Nesbitt, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. John E. Ashby, 3622 Fairmount Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

HOUSTON PEDIATRIC SOCIETY

President: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Fred Ames, Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION, PEDIATRIC SECTION

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alexander T. Martin, 107 E. 85th St. New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. W. E. Chapin, 1001 E. Clay St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Samuel Levin, 2501 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April